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THE EFFECT OF PYLORECTOMY ON CANINE ANTRAL-DUODENAL CO-ORDINATION AND GASTRIC EMPTYING

by

© H. FREDERICK GIVEN

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH IN

PARTIAL FULFILMENT OF THE REQURIEMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

IN

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DEPARTMENT OF SURGERY

EDMONTON, ALBERTA

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THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled THE EFFECT OF PYLORECTOMY ON CANINE ANTRAL-DUODENAL CO-ORDINATION AND GASTRIC EMPTYING submitted by H. FREDERICK GIVEN in partial fulfilment of the requirements for the degree of MASTER OF SCIENCE IN EXPERIMENTAL SURGERY.

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Date: 9th May 1980.

DEDICATION

TO KATHRYN

AD MULTOS ANNOS

The more I read, the more I meditate;

and the more I acquire, the more

I am enabled to affirm that I know nothing.

- Voltaire

A B S T R A C T

No studies have been reported to date in which gastric emptying, gastro-duodenal electrical and mechanical contractile activity, and canine pyloric pressure have been measured simultaneously. The purpose of this study was to investigate these parameters before and after pylorectomy in 5 conscious dogs.

Four sets of bipolar recording electrodes and miniature strain gauges were attached to the serosa at 7 and 5 cm proximal and distal to the pylorus. For measurement of gastric emptying a modified Thomas cannula was inserted percutaneously into the duodenum 15 cm distal to the pylorus. The solid and liquid phases of the meals were measured using ^{99m}Tc labelled chicken liver and polyethylene glycol (PEG) in water collected via the Thomas cannula.

One dog had an omnipresent, abnormally fast, antral electrical control activity (18 - 20/min) and on recordings the waves were propagated in an orad direction. Emptying of both solids and liquids was apparently slower when compared with the four "normal" dogs. The antral electrical control activity and gastric emptying returned to normal following pylorectomy. Code (1974) described a similar increase in the rate of the electrical control activity in a dog, over short periods. He called it tachygastria.

In four dogs the rate of gastric emptying was related to the force and frequency of antral contractions. Antral-duodenal co-ordination was disrupted by pylorectomy. This resulted in loss of relationship between duodenal electrical response activity and antral electrical control activity post-prandially. A reduced antral motility index also resulted. The mechanism involved was believed to be an intrinsic myo-neural feedback mechanism from the duodenum.

The balance of evidence in this investigation also suggests that the canine pyloric ring is not a tonically contracted sphincter which opens only occasionally, but that it behaves as the distal end of the thickened antral muscle mass.

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CHAPTER I

The object of this study was to make simultaneous measurements of gastric emptying and recordings of gastric motility in conscious dogs, and thereby to correlate transit of solids and liquids with motility.

The stomach has three major motor functions:

a) it accommodates liquids and solids and its capacity can vary in response to changes in intraluminal pressure. This occurs mainly in the fundus and body.

b) it mixes and grinds food producing a semisolid suspension. This occurs mainly in the body and antrum.

c) it propels the mixture into the duodenum. The propulsion occurs in the antrum.

The pylorus, at the terminal end of the antrum, has a narrow lumen and a thickened muscle layer. As reviewed by Edwards and Rowlands (1968) there are two opposing views concerning the function of the pyloric region. On the one hand it is presumed to be a sphincter which regulates transit from the stomach to the duodenum, and on the other hand it is believed to be merely the terminal end of the antrum, with similar motor functions as the remainder of the antrum. This question was explored in the present study by assessing the effects of removing the pylorus.

CONTROL OF MOTILITY

• Gastric motility results from intrinsic myogenic activity and is influenced by neural and hormonal mechanisms.

Myogenic Electrical Activity. Gastrointestinal smooth muscle exhibits two types of electrical activity, namely electrical control activity (ECA) and electrical response activity (ERA) (Daniel and Irwin, 1968). Electrical control activity is also called pacesetter potential, basic electrical rhythm, or slow waves; while electrical response activity is known as spike potential, spike activity, or fast activity (Carlson et al., 1968; Kelly et al., 1969).

Electrical control activity is an omnipresent cyclical change in electrical potential which can be recorded even in the absence of visible contractions. Species differences in the rate of these contractions have been reported. Rhythmic contractions in un-anaesthesized man occur at 3/min. (Daniel and Chapman, 1963; in the unanaesthesized dog at 5/min. (Carlson et al., 1966); in the cat at 3-4/min. (Bartoff and Weg, 1965); and in the rat at 4-5/min. (Armitage and Dean, 1966). Anaesthesia and changes in body temperature cause slight variations in periodicity (Carlson et al., 1966). It is important to realize that electrical control activity is an electrical phenomenon and does not produce muscle contraction.

The second type of activity, the electrical response activity, is

the activity associated with contractions (Daniel and Irwin, 1968). It consists of rapid oscillations of short duration, arising during the depolarization phase of the electrical control activity. The resting stomach, therefore, exhibits electrical control activity only, whereas the contracting stomach exhibits both electrical control activity and electrical response activity.

The electrical control activity originates from a site on the greater curvature of the stomach, close to the junction of its middle and orad thirds (Kelly and Code, 1971). This activity arises from the smooth muscle of the gastric wall and is therefore myogenic rather than neurogenic in origin. This statement is based on the knowledge that electrical control activity can be recorded from excised and therefore centrally denervated segments of stomach (Prosser and Bortoff, 1968), after nerve conduction blockade with tetrodotoxin (Job, 1969). Electrical control activity is recordable from thick amnion which is devoid of nervous tissue (Prosser and Rafferty, 1956). In the cat colon, it originates in the circular muscle (Christensen et al., 1969), but in man and the dog it appears to arise in the longitudinal muscle (Caprilli and Onori, 1972).

Generation of the electrical control activity is an inherent property of the muscle of the distal half of the stomach and propagation appears to be direct from one muscle cell to the next without involvement of neural elements (Sarna et al., 1971). The direction of normal pro-

pagation, i.e. aborad, has been explained in terms of an array of bidirectionally coupled relaxation oscillators with those most proximal having the fastest intrinsic frequency (Sarna et al., 1972). Since the fundus and proximal stomach appear to be electrically inactive, the dominant pacemaker of the normal stomach is found at the most proximal point of the electrically active region. Propagation of the slow wave is therefore, exclusively distal.

Sarna et al., (1972) prefer to call this site the most proximal site of electrical control activity (MPSECA). They feel that the term pacemaker is misleading since it implies that the control wave in this region conducts to the rest of the stomach as in an electric cable. The pacemaker in the stomach has no special properties other than being the fastest intrinsic frequency of oscillation.

Experimentally, it is possible to produce retrograde peristalsis from an artificial pacemaker, implanted in the distal antrum or proximal duodenum (Kelly and La Force, 1972). There is no evidence, however, that retrograde peristalsis ever occurs naturally.

The electrical control activity in this manner synchronizes and governs the contraction of gastric muscle by establishing the moment when it may occur. However, the factors which determine whether or not contractions occur are less precisely defined. Neural and hormonal influences are recognised to be modulators of electrical activity.

Neurogenic Control. Motor fibres of the vagus are of two main types, one excitatory and one inhibitory. The excitatory are cholinergic, whereas the inhibitory are neither cholinergic nor adrenergic and their neurotransmitter is unknown. Burnstock (1972), proposes a purine nucleotide transmitter but on current evidence this seems unlikely (Mir et al., 1979).

In addition to these two main categories of motor neurones the vagus also contains some adrenergic fibres with sympathetic activity. The main sympathetic efferent innervation of gastric muscle comprises post-ganglionic fibres from the coeliac and splanchnic ganglia which connect with lower thoracic segments of the spinal cord. Adrenergic inhibitory neurones and cholinergic excitatory neurones are present (Heading, 1979). These sympathetic and parasympathetic neurones form the efferent limbs of reflexes which regulate gastric contractility. These nerves terminate in neural plexuses within the wall of the stomach. The neural plexuses thus serve as communication centres of the autonomic innervation. They facilitate or inhibit the occurrence of muscle contraction in association with electrical control activity and are the means of co-ordinating contraction to form peristaltic waves. The propagation of contraction is therefore dependent on the integrity of the neural plexus, whereas propagation of the electrical control activity itself is not (Heading, 1980). Nevertheless, the electrical control activity is influenced to some extent by autonomic

innervation. For example, propagation is temporarily disrupted and permanently slowed by vagotomy (Kelly and Code, 1969). The organisation of neuronal control of motility across the gastro-duodenal junction was studied by Sarna and Daniel (1976). They showed that electrical stimulation of the anterior or posterior nerve of Latarjet caused distal antral contractions and transient inhibition of spontaneous duodenal contractions. Their study, in fact, shows that nervous mechanisms under vagal control can both inhibit and excite proximal duodenal contractions and provide a basis for co-ordination of sequential antral-duodenal contraction.

Hormonal Control. The effect of gastrointestinal hormones on gastric emptying may be either physiological or pharmacological. Cholecystokinin (CCK) and secretin retard gastric emptying physiologically since the doses are less than the D_{50} dose for pancreatic secretion (Debas et al., 1975; Valenzuela, 1976). Although gastrin (Hunt and Ramsbottom, 1967), secretin (Vagne et al., 1968; Chey et al., 1970; Sugawara et al., 1969), and CCK (Yamigishi and Debas, 1978; Sugawara et al., 1969), all reduce gastric emptying, the mechanism of their actions is different.

Gastrin increases electrical control activity, antral electrical response activity and contractions, inhibits fundal phasic contractions and reduces pyloric contraction in response to duodenal acidification (Kwong et al., 1972; Cooke et al., 1972; Fisher and Boden, 1976).

Secretin decreases antral motility but increases pyloric pressure (Kwong et al., 1972; Fisher et al., 1973).

CCK, in vitro, stimulates antral and fundal contractions (Gerner et al., 1977). In vivo, however, CCK has an inhibitory effect on antral motility.

Glucagon causes inhibition of gastric motility but only at pharmacological doses. Motilin increases gastric emptying of liquids in dogs and this action is not blocked by vagotomy or antrectomy (Debas et al., 1977). When motilin is infused during the interdigestive state in dogs it induced a pattern precisely like the naturally occuring interdigestive contractions (Itoh et al., 1976). It is the only substance known to be active during the interdigestive state and therefore, may be called the interdigestive hormone.

Other gastrointestinal hormones may effect gastric motility. Not enough is known at present however, to enable a realistic assessment of the relative importance of these hormonal factors on gastric emptying.

RELATIONSHIP BETWEEN CONTRACTIONS AND EMPTYING

The relationship between peristaltic contraction of gastric muscle and emptying of gastric contents is complex. Emptying requires co-ordination of motility in the antrum, pylorus and duodenum. Some "retropulsion" is also associated with normal antral peristalsis.

Indeed the balance, between forward propulsion of the antral contents through the pylorus, and their retropulsion towards the gastric body, is determined by the nature, force, and longitudinal extent of antral contractions and by the timing of pyloric opening. In view of this, the absence of a clear relationship between emptying and the relatively crude measurement of "antral motility" presently available, is hardly surprising.

The Antrum. Antral contraction is responsible for the grinding and mixing of gastric contents before they are delivered to the duodenum. This grinding and mixing is termed the "antral mill". The consistency of the chyme emptied through the pylorus is determined by antral propulsion and retropulsion. This occurs because solid particles are preferentially retropulsed. Solid particles must be greater than 2 mm in diameter before differentiation from the fluid component of the gastric contents is made (Meyer et al., 1979).

Despite the preferential retropulsion of solid particles, inert materials, resistant to the grinding action of the "antral mill", will eventually pass into the duodenum provided that they do not cause pyloric obstruction.

The Pylorus. The pylorus is recognised as a distinct anatomical entity, marking the gastric outlet into the duodenum. The movement

of luminal contents through the pylorus occurs in one direction only, stomach to duodenum, both during emptying of a meal and in the resting stomach. Hence, the pylorus is considered to be a sphincter.

Functionally, the pyloric muscle is part of the antro-pyloro-duodenal propulsive mechanism. Co-ordination of the antrum, the pylorus, and the duodenum is important in the control of the rate of gastric emptying. The pylorus was initially believed to act as an electrical insulator, but studies on animals (Bortoff and Davis, 1968), and in man (Duthie et al., 1971), have shown that antral electrical control activity spreads across the pylorus into the proximal duodenum. This transmitted antral electrical control activity augments the duodenal electrical control activity, bringing the duodenal cells closer to their critical level for de-polarization and hence increasing the probability of duodenal electrical response activity. The relationship is abolished by complete pyloric transection (Bedi and Code, 1972), but not by denervation of the area. This indicates that co-ordination is myogenic rather than neurogenic in origin.

During duodenal contraction the pylorus is closed and reflux of duodenal contents into the antrum is prevented. Following duodenal contraction, the duodenal, pyloric and antral muscles relax so that the pylorus is no longer closed. Because there is no pressure gradient from duodenum to antrum, there is no reflux of duodenal fluid into the stomach. At present there is no general agreement that the

resting pylorus has a higher pressure than that of the antrum or duodenum. The pylorus, therefore, does not fulfil the criteria for a physiological sphincter. It would appear that the pylorus should be regarded simply as the distal part of the gastric antrum (Heading, 1980).

Normal pattern of Gastric Emptying. The emptying of a normal stomach approximates to a simple exponential pattern (Hunt and McDonald, 1954; Hunt and Spurrell, 1951). Hopkins (1966) shows however, that the pattern of gastric emptying reflects more precisely the square root function of the volume of the meal remaining in the stomach. This occurs whether the meal consists of carbohydrates, fats or proteins (Borgstrom et al., 1957), or even whether solid or compliant spheres are used (Schlegal et al., 1966). Is such a simple relationship to be expected, given the number of variables and their determinants; or does it reflect poor experimental resolution of data?

Cannon (1898) first proposed that liquids are promptly emptied from the stomach into the duodenum, whereas solids are retained for continued mixing and grinding. In 1966, Carlson et al., using plastic spheres, have shown that the antrum normally controls the emptying of these spheres by propelling a few at a time into the duodenum while retropelling the majority into the proximal stomach during antral contractions.

Experiments were undertaken with radiolabelled chicken liver by Meyer et al., (1976) and their findings agreed with other workers (Hinder and Kelly, 1977; Heading et al., 1976; Thomas and James, 1957), that early and rapid separation of liquid and solid components of a meal occurred with the liquid component emptying rapidly while the solid component emptied more slowly. They also found that neither the volume of the liquid component of the meal nor the rate of its emptying affected the emptying of the solid component - this agreed with previous findings (Hinder and Kelly, 1977). The latter found that homogenization of the meal speeded its emptying.

All the findings to date show that liquids are emptied faster than solids; that the stomach can discriminate and exclude pieces of food larger than 2.0 mm. from emptying, and that slower emptying of foods above this size is in fact the result of the delay required to reduce the larger food to the size range permitted to pass.

REGULATION OF GASTRIC EMPTYING

Gastric emptying is influenced by a variety of physical and chemical properties of an ingested meal. The complexity of the responses of a variety of stimuli render it difficult to assess their relative importance. Volume, fat content and energy density of a meal however, seem likely to be the dominant factors in regulating emptying in normal subjects.

Intragastric volume. Increasing the gastric volume excites the slowly adapting mechanoreceptors, which in turn cause receptive relaxation of the fundus and body of the stomach (Leek, 1972). This enables increased volume to be accommodated without an increase in intra-gastric pressure. The receptive relaxation is mediated via the vagal nonadrenergic inhibitory nervous system (Jansson and Martinson, 1965). There is an established relationship between intra-gastric volume and gastric emptying. Indeed, gastric distension is the only physiological stimulus known to accelerate emptying (Hunt and Knox, 1968).

Energy Content of Meals. Hunt and Stubbs (1975), have observed that the greater the nutritive density of a meal, the slower the emptying. McHugh and Moran, (1979), have shown that regulation of gastric emptying by caloric density is very precise. Isocaloric (0.5 K cal/ml) meals of glucose, casein, hydrolysate and medium chain triglycerides emptied at the same rate. However, when the glucose concentration exceeded 1.0 K cal/ml gastric emptying did not slow further and isocaloric regulation was lost.

Osmolarity. In 1905, Carnot and Chassevant observed, that isotonic saline solutions repeatedly emptied from the stomach more quickly than

hyper-osmolar or hypo-osmolar solutions. This work has since been repeatedly confirmed (Apperly, 1926; McSwiney et al., 1938). The osmoreceptors, which slow gastric emptying, are present in the duodenum and not in the jejunum or stomach (Shay et al., 1942; Hunt, 1963; Meeroft, 1975).

Acids. Intra-duodenal acids inhibit gastric emptying; the magnitude of the effect being proportional to the acid concentration. There appear to be receptors responding to acids located in the proximal duodenum, and their influence on emptying is mediated neurally (Cooke, 1974).

Fats. Fatty acids are extremely potent inhibitors of gastric emptying. Hunt and Knox (1968), studied the effects of various chain lengths of a large variety of salts of fatty acids and found that the acids fall into two groups. From C_2 up to C_{10}, acetic to decanoic increase in chain length has little influence on effectiveness of gastric emptying. These are the fatty acids which are mainly absorbed into the portal blood (Bloom et al., 1951). From C_{12} to C_{18} the salts of the fatty acids are about four times more effective than the short chain group, C_{14} (myristic) being the most effective. These are the acids which are esterified in the mucosa of the small intestine, myristic in particular and pass into the lymph as triglycerides (Bloom et al., 1951, Gelb and Kessler, 1963). Although receptors are believed to lie in the walls

of the duodenum, no structures which are recognisable as such have been reported (Hunt and Knox, 1968).

Amino Acids. Cooke and Moulang (1972), have studied the effects of amino acids on gastric emptying. They found that all amino acids in concentrations of 0.2 M, delayed emptying significantly. They suggest that emptying of amino acids may be under the control of osmoreceptors in the duodenum.

ABNORMALITIES OF GASTRIC EMPTYING

Gastric Surgery. Vagotomy, of one kind or another, is a part of most operations now in use for the surgical treatment of peptic ulcer disease. McCrea et al., (1927), and Hughson (1927), from their work, believed that truncal vagotomy had little permanent effect on gastric motility. After an initial period of inhibitional paresis, a decrease in the initial emptying time was the only pronounced and constant finding reported by these authors. Meek and Herrin (1934), showed that following thoracic vagotomy in the dog, gastric emptying of a diet of milk or biscuits with barium, was slowed significantly. This change persisted for at least five months and they believed it to be permanent.

When Dragstedt and Camp (1948), encountered clinically significant stasis after performing truncal vagotomy alone, they added gastro-

jejunostomy as a drainage procedure to permit adequate gastric evacuation. Thus, subsequently, the operation of vagotomy has been accompanied by a drainage procedure.

However, with pyloroplasty, the delicate pyloroduonal mechanism is destroyed and can never be reconstituted, while gastro-jejunostomy simply by-passes this region. Either of these operations in combination with vagotomy converts a delicate storage and pumping mechanism controlled by fine neuro-facilitatory and inhibitory impulses, into a denervated bag which empties precipitantly through a large hole in its wall (Kelly and Kennedy, 1975). It is this factor that may produce the post-operative complication of diarrhoea and dumping following vagotomy and drainage procedure (Goligher et al., 1972).

It is now known that pyloroplasty or antrectomy without vagotomy does not affect significantly the emptying rates of either solids or liquids (Yamagishi and Debas, 1978; Gleysteen et al., 1976). Dozois et al., (1971), however, showed that distal antrectomy i.e. excision of a 3.5 cm of segment of distal antrum including the pylorus markedly speeded the discharge of radio-opaque plastic spheres into the stomach. This procedure did not affect significantly the emptying rate of liquids.

From the work of Dragstedt and Owens (1943), it was shown that truncal vagotomy produced gastric stasis in man. Burge et al., (1969) suggested that selective vagotomy without a drainage procedure is not followed by gastric retention if duodenal stenosis is absent. However,

Shina and Griffith (1969), Kilby and Griffith (1971), have proven that selective vagotomy without a drainage procedure causes gastric retention in dogs. In man selective vagotomy without a drainage procedure has been abandoned because of gastric stasis even when duodenal stenosis has been excluded (Franksson, 1948; Clarke et al., 1972).

In 1957 Griffith and Harkins suggested that gastric stasis could be avoided after vagotomy if the nerves to the antrum were preserved. Amdrup and Jensen (1970), and Johnston and Wilkinson (1970), following their clinical trials have suggested that post-operative sequelae could be minimized or abolished by performing a proximal gastric vagotomy without a drainage procedure. It has now been shown by a number of workers (Walker et al., 1974; Geurts et al., 1977; Brandsborg et al., 1977) that proximal gastric vagotomy has minimal disruptive effect on the antral-duodenal relationship and it has little significant effect on gastric emptying time. Hinder and Morris (1978), state that rapid initial emptying of a milk meal occurs after truncal vagotomy and proximal gastric vagotomy, but the subsequent pattern of gastric emptying is more normal after proximal gastric vagotomy than truncal vagotomy.

McKelvie (1970), Colmer (1971), Cobb et al., (1971) and Wilkinson and Johnson (1972), Gleysteen et al., (1976) have all shown

that a truncal vagotomy or a selective vagotomy and pyloroplasty results in very rapid initial gastric emptying. When pyloroplasty is added to vagotomy a significant increase in the rate of gastric emptying occurs and a drainage procedure is best avoided to avoid postoperative dumping.

Hinder and Bremner (1978), showed 51-63% decrease in intragastric volume in the first 10 minutes after a milk meal and that the speed of emptying is proportional to the original meal volume. Therefore, the therapy of treating postoperative dumping and diarrhoea with frequent small meals seems rational.

Truncal vagotomy temporarily disorganises the orderly gastric electrical control activity and permanently slows its propagation (Kelly and Code, 1969). Proximal gastric vagotomy causes episodes of disorganised electrical control activity (Wilbur and Kelly, 1973). Truncal vagotomy reduces antral contractile activity measured by extraluminal strain gauges, while proximal gastric vagotomy virtually unalters it (Walker et al., 1974).

Bass et al., (1979) have shown that removal of the duodenal bulb causes immediate disruption of the normal antral electrical and antral duodenal motor activity. The antral electrical arrythmias decrease with surgical recovery but the normal antral duodenal electrical and motor relationship remain disrupted.

In conclusion, only proximal gastric vagotomy causes minimum disruption of the antral duodenal relationship. Contractional activity of the antrum has the same pattern before and after proximal gastric vagotomy and should be considered at the present as the most physiological operation for surgical management of peptic ulcer disease.

Peptic Ulcer Disease. Gastric emptying may be disturbed by many and varied clinical conditions (Rimer, 1966). Pyloric outlet obstruction caused by such conditions as idiopathic hypertrophic pyloric stenosis, chronic duodenal ulcers, polyps, carcinoma, will cause delayed gastric emptying.

Information about the rate of gastric emptying in patients with duodenal ulcer has been contradictory (Hurst, 1920; George, 1968; Bromster, 1969; Hunt, 1957), but recent studies have shown that the majority of patients with duodenal ulcers empty solids (Shay et al., 1942; Griffith et al., 1966; Griffith et al., 1968; Fordtran and Walsh, 1973), and fluids (Lagerluf et al., 1960; Wormsley, 1972) more rapidly than normal subjects. Patients with gastric ulcer empty food normally (Buckler, 1967), while liquid test meals are emptied at the same rate (Griffith et al., 1968), or at a slightly slower rate than normal (George, 1968).

The mechanism causing increased gastric emptying in duodenal ulcer patients is not known (Wormsley, 1974), but it may be connected with

abnormally high partial pressure of carbon dioxide found in the duodenum of these patients (Rune, 1972). It has been shown by Wormsley (1973), that a high p CO_2 in the duodenum increases the rate of gastric emptying.

Whether the abnormal gastric emptying seen with duodenal ulceration is a result of the ulcer or a factor in its causation, is still unknown.

OBJECTIVES OF PROJECT

There have been no studies reported in which gastric emptying, gastroduodenal electrical and mechanical contractile activity, and canine pyloric pressure, have been measured simultaneously. The objective of this study was to measure all of these parameters simultaneously in the dog, in an attempt to answer:

1. Does the pylorus play any part in emptying of liquids as well as solids?
2. Can the mechanical activity, electrical activity and intraluminal pressure across the gastroduodenal junction be correlated?
3. Is it possible to detect changes in these activities in relation to emptying of liquids and solids?
4. What are the effects of pylorectomy?

CHAPTER II

MATERIALS AND METHODS

EXPERIMENTAL DESIGN

Healthy, female, adult, mongrel dogs, which had been rendered free of intestinal parasites and had received antirabic and distemper vaccines were used. Their weight varied from 19 kg to 25 kg. The dogs were fed a special high protein diet preoperatively, and again postoperatively.

The dogs remained healthy during the experimental period. All observations were made in the fully conscious dog. The dogs were trained to rest quietly in a Pavlov type stand, partially or completely supported by a canvas sling, throughout recording sessions.

At the initial operation miniature strain gauges, bi-polar electrodes and a modified Thomas cannula were implanted in each animal.

Construction of Recording Devices. Gastric motility recording devices were constructed (Figure I). A single device contained three force strain gauges EA series (Micro-Measurements, Romulus, Mich.), each encased in a silastic mount with 36-gauge Teflon covered silver wire attachments extending 30 cms to a socket. The lead wire, plus silastic mount, were encased in a silastic tube which was filled with silicone. The lead off wires were connected to an Amphencol plug (222-12N 19↓),

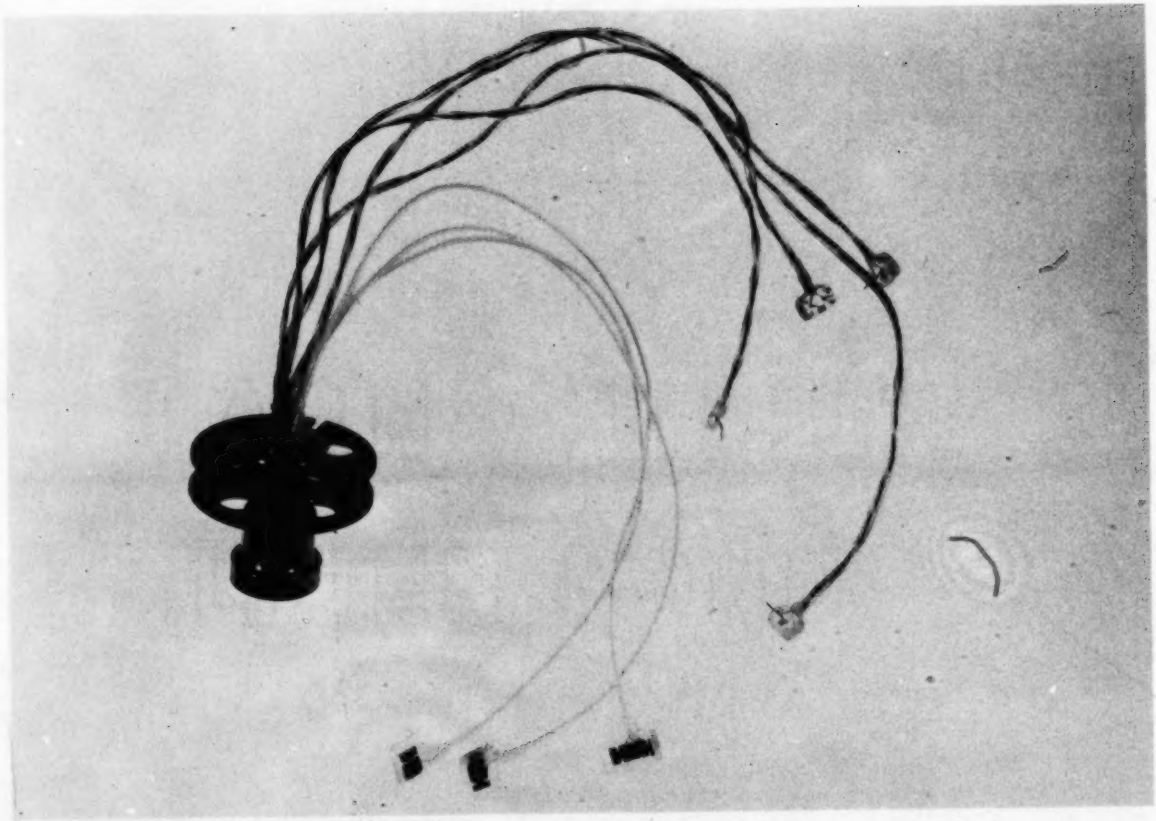

FIG. I. GASTRIC MOTILITY RECORDING DEVICE SHOWING TITANIUM CANNULA WITH 4 BIPOLAR ELECTRODES AND 3 STRAIN GAUGES ATTACHED.

sealed with beeswax and embedded with dental acrylic in a titanium biflanged cannula.

The device also contained four bipolar electrodes constructed of 10% platinum irridium wire, diameter .381 mm. The electrodes were connected to a teflon coated silver wire, encased in a silastic base. The electrodes, plus their connection to the silver wire, were embedded in epoxylite 751 resin (Lee Pharmaceutical) rectangular mould 10 mm by 5 mm by 2mm. The electrodes protruded 2mm from the mould; all four had similar wire attachments to the socket.

Design of Cannula. The Thomas cannula was re-designed (Figure II) in order to facilitate retrieval of perfusion catheters from the bowel lumen. A tightly fitting titanium plug was made for the cannula. This was maintained in place in the cannula by a metal cap. On the plug were three metal prongs, to which the catheters could be attached.

Construction of Perfusion Catheters. The perfusion catheters consisted of 3 silastic tubes (Dow Corning I.D. .635 mm by 1.194 mm O.D.) bonded together and marked radiopaquely. There was one side orifice, 1.2 mm in diameter, in each tube and they were spaced 5 cms. apart.

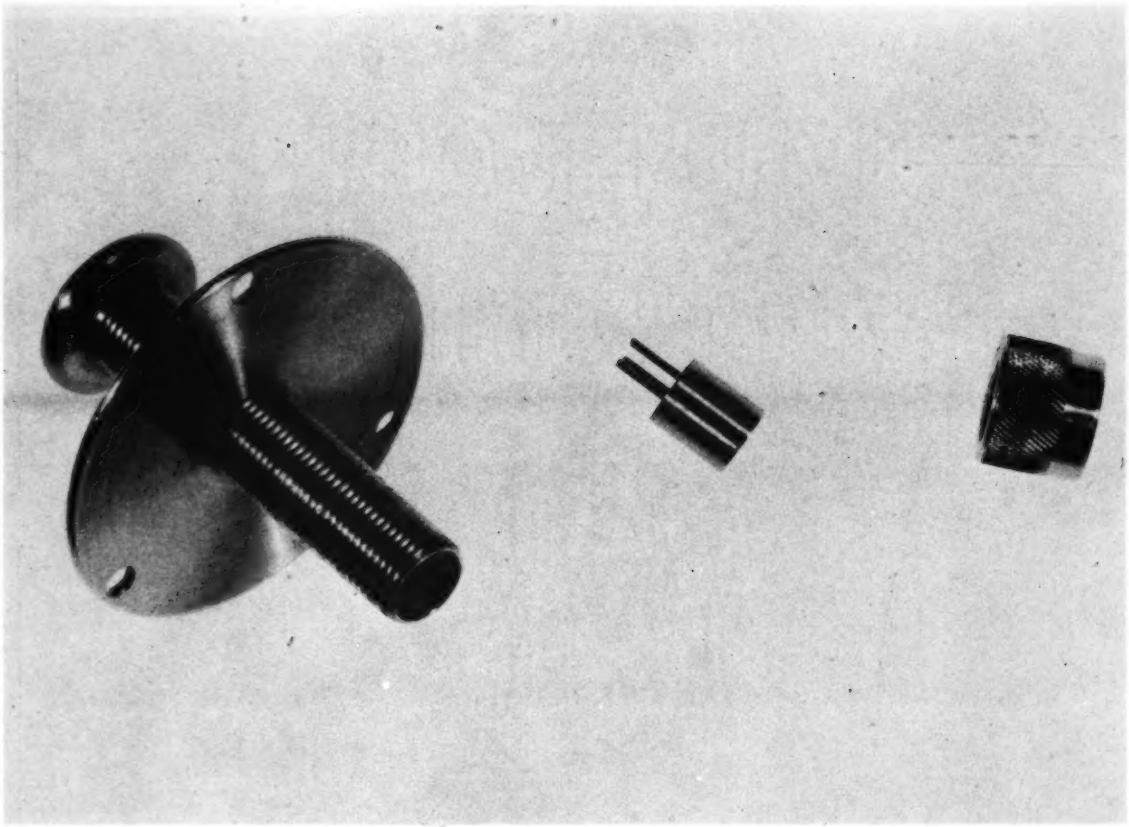

FIG. II. CANNULA FOR CONNECTING SUBCUTANEOUSLY, IMPLANTED PERFUSION CATHETERS.

Operative Technique. The implantations were performed while employing the usual surgical sterile precautions. The dogs were anaesthetized with an intravenous injection of Sodium Pentobarbital 30 mg/kg (Diabutal, Diamond Laboratories, Calgary, Canada). An endotracheal tube was inserted and the animals were maintained on air for the duration of the surgery. A bolus dose of 60 mg of Sodium Pentobarbital was given during surgery to maintain adequate anaesthesia if required.

Laparotomy was performed for implantation of motility recording devices through an upper midline incision. The gastroduodenal junction was identified by palpation of the thickened pyloric ring, and by identification of the depression and veins on its surface. The three strain gauges were sutured with 4/0 silk to the gastroduodenal serosa, greater curve border, 5 cm proximal and 5 and 6.5 cms distal to the gastroduodenal junction (Figure III). The two bipolar duodenal electrodes were sutured adjacent the duodenal gauges; the two antral electrodes were sutured one adjacent to the antral strain gauge and one 6.5 cm proximal to the gastroduodenal junction. The wire attachments to the gauges and electrodes led through a stab wound, 2 inches to the left and lateral to the midline incision, to the plug which was sutured to the abdominal parietes and emerged through a cutaneous stoma. A socket counterpart could then be connected to this plug with wires leading to a recorder for monitoring of electrical and mechanical activity.

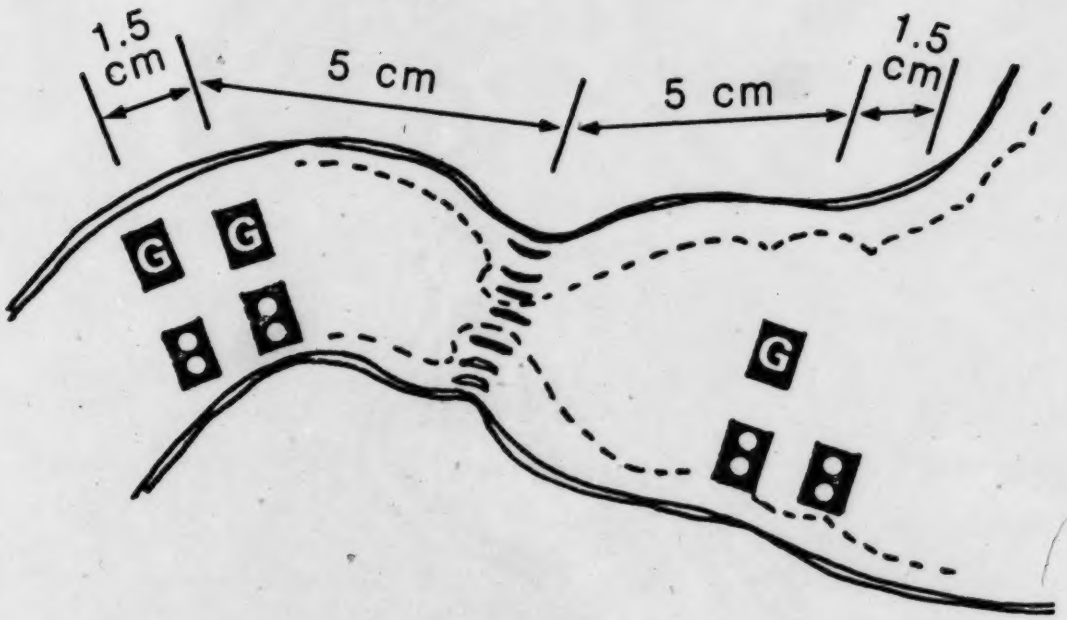

FIG. III. POSITION OF 4 BIPOLAR ELECTRODES AND 3 STRAIN GAUGES (G) ON ANTRUM AND DUODENUM.

A chronic duodenal fistula was made in each dog by placing the modified Thomas cannula in the duodenum 15 cms. distal to the gastroduodenal junction (Figure IV). A segment of arterial graft Dacron mesh 2 cms long and of suitable diameter was transected longitudinally and sewn around the duodenum just distal to the cannula. This technique was used in the first two dogs only. It was used since it was believed that this method facilitated a watertight seal between bowel wall and the balloon of a Foley's (Size 12) catheter inserted via the duodenal cannula in a caudad direction into the bowel lumen and inflated with 10 ml of air beneath the dacron cuff. However, following measurement of gastric emptying with and without the Foley's catheter in situ no significant difference in emptying was demonstrated. Hence the dacron cuff and Foley's catheter were not used in the remaining three dogs. The Thomas cannula was brought through a right stab wound 2 inches lateral to the midline incision and the cannula was fixed in situ by means of the flange washers. The perfusion catheters were sited and fixed by suturing with surgical steel 000 during operation, through a small gastrostomy opening (< 2 cm). This gastrostomy was situated in the distal third of the body of the stomach. The perfusion catheters were thus fixed so that one opened in the antrum, one in the pylorus, and one in the duodenum.

The creation of the duodenal fistula served for collection of the duodenal contents during gastric emptying of both solids and liquids.

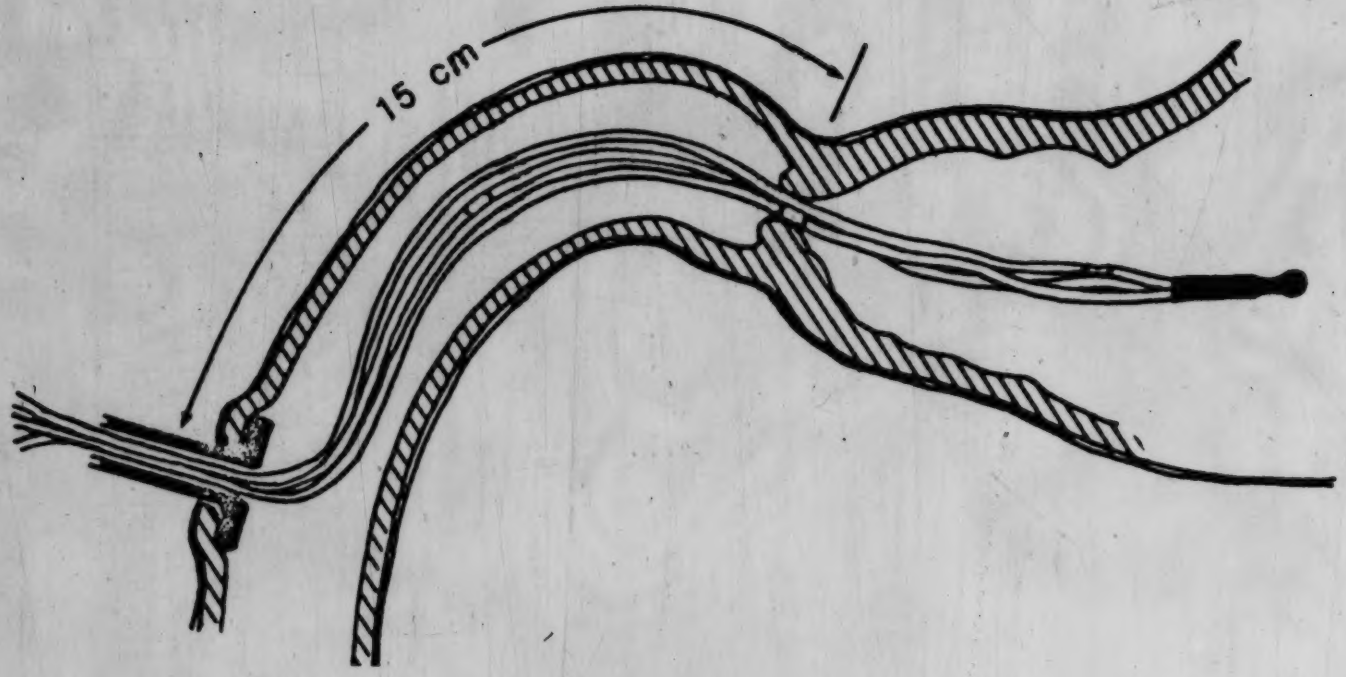

FIG. IV. CANNULA AND PERFUSION CATHETERS IN SITU IN DUODENUM

It also facilitated the retrieval of the perfusion catheter from the duodenum during recording sessions, in order to measure the intraluminal pressures.

Methods of Recording. Following operation the dogs were allowed one week in which to recover before recordings were commenced. Recordings were made in each dog for a minimum of 4 hours daily following a twenty-four hour fast. The conditions during recordings were standardized. The dogs were placed in the Pavlov sling. A socket counterpart was then connected to the plug in the dogs abdomen, with wires leading to an 8-channel Beckman Type RM Dynograph recorder for monitoring of electrical and mechanical activity. The strain gauges were connected to the recorder through strain gauge couplers type 9803, while the electrodes were connected to the Beckman through A-C couplers type 9806A with a time constant of 1 second. Respiration was recorded by means of a wish-bone type pneumograph strapped around the dog's chest and connected by means of a strain gauge coupler 9803 to the Beckman recorder.

The perfusion tubes were perfused with water (0.35 ml/min) by means of a low compliance pneumohydraulic pump and connected through Statham transducer (p 33 BB) to strain gauge couplers type 9872 on a second Beckman Type R M 8 channel recorder.

Recordings of electrical, mechanical and intraluminal pressures were simultaneously recorded from the Beckman recorders on to a magnetic tape (AMPEX BACKCOATED I MIL TAPES 1/2 inch) for computer analysis.

FEEDING EXPERIMENTS

Recordings were taken for 60 minutes (minimum) while the animals were fasting. The dogs were then offered 300 ml. of water containing polyethylene glycol (PEG) 4000, in the concentration of 1,000 mg/dl. The amount of water consumed was determined by weighing the feeding dishes before and after feeding. At feeding the dog was also offered 40 - 50 G. of radiolabelled chicken liver mixed with 100 G of canned dog food (Dr. Ballards). If any meat was not consumed (never more than a trace), the uneaten meat in the dish was collected and counted and its total count subtracted from the calculated counts fed. Dogs varied widely in their consumption of water. The volume of liquids given was varied from 100 ml to 600 ml to study the effects of distension of the stomach on the emptying of a solid meal, and also on the emptying of liquids.

A minimum of four recordings and measurements of gastric emptying were made in the second post operative week.

Radiolabelling of Food. The radiolabelled chicken liver was prepared each morning immediately before recording by the technique described by Meyer et al., (1976; 1979).

Technetium sulphur colloid ^{99m}Tc 80μCi was injected intravenously into the wing vein of a live chicken. After 30 minutes the chicken was killed by crushing the cervical spinal cord, and the liver was removed and washed. The washed liver was homogenized and mixed with 100 G of standard canned dog food (Dr. Ballards). Technetium is used because after intravenous injection the colloid is phagocytized uniformly by the Kupffer cells throughout the liver (Horner, 1966). Approximately 60% of the injected radioactivity was localized in the chicken liver in this time interval and, as judged by the specific activity (counts/g), the ^{99m}Tc was uniformly distributed in chicken livers prepared in this fashion. The total counts fed to the dogs were calculated, by determining the average specific activity of four representative pieces of the liver plus canned food, and multiplying this figure by food (grams) consumed. Glass tubes, filled to a standard height with collected chyme, were placed in a Well Crystal Counter (Picker Pace I) and the radioactivity measured.

For three hours from the start of the feed all material exiting from the uncorked duodenal fistula was collected every 15 minutes. The total amount collected was measured, a 2 ml sample was sent for ^{99m}Tc count and two 5 ml samples were sent for PEG estimation.

PEG Estimation. PEG was estimated by the improved turbidimetric analysis utilizing an emulsifier as described by Malawer and Powell (1967). The use of this material for intestinal studies was first suggested by Shaffer and Critchfield (1949) who demonstrated its quantitative passage through the gastrointestinal tract. It was first used by Sperber et al., (1953) in animals, and by Borgstrom et al., (1957) in men. The method, based on the gravimetric and colormetric determination of PEG concentration, was tedious and time consuming. Hyden (1955) introduced a turbidimetric analysis based on the development of an oil-in-water emulsion of PEG when it was exposed to trichloracetic acid in the presence of barium ions. Malawer and Powell (1967) have made the determination highly accurate and reproducible by adding an emulsifying agent, gum arabic. This stabilised the oil-in-water emulsion and hence eliminated the need for precise timing.

PYLORECTOMY

The dogs were then subjected to a second operation in which the pylorus (approx. 1.5 cms. of tissue) was excised (Figure V). This operation was performed through the previous mid-line incision. Care was taken not to disturb the previously implanted strain gauges or electrodes. A conventional one layer anastamosis with 2/0 catgut was performed. Again, as in the previous operation, the dogs were anaesthe-

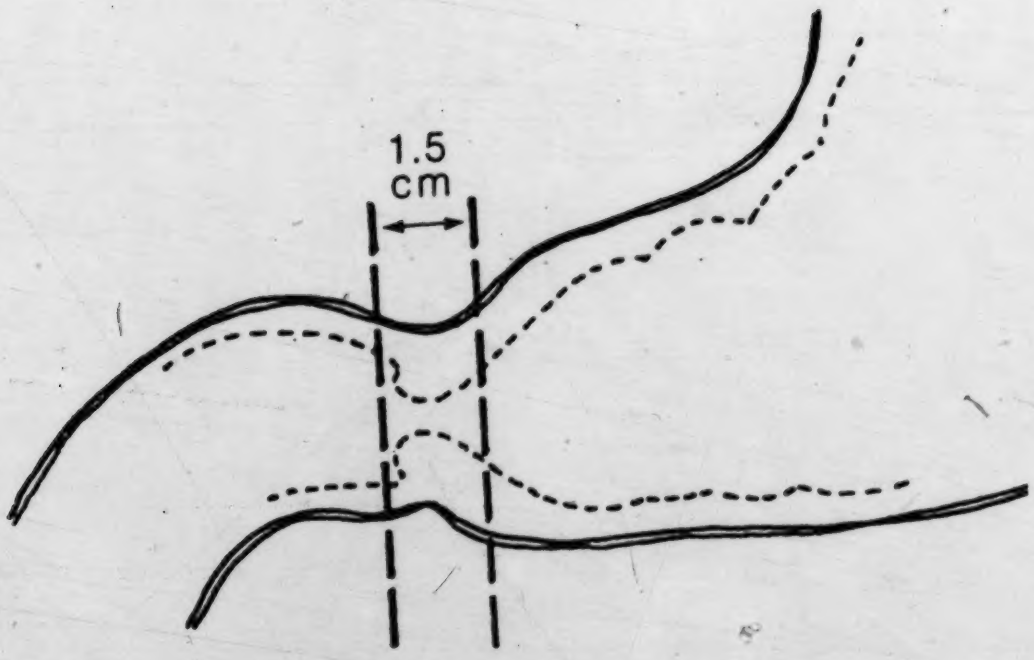

FIG. V. EXCISION OF PYLORIC RING

tized with Sodium Pentobarbital, intubated and given Dextrose/saline 5 ml/kg/hour during the operation.

The dogs were given one week in which to recover post-operatively prior to commencement of recordings and measurement of gastric emptying. These parameters were then measured in each dog at least twice weekly until failure of the strain gauges or electrodes occurred.

After completion of studies in each dog, the animal underwent necroscopic examination of the stomach, duodenum, gauges and electrodes.

CALCULATION OF RESULTS AND STATISTICAL ANALYSIS

STATISTICAL ANALYSIS

The emptying rates obtained were normalized to the percent of ^{99m}Tc labelled liver or PEG fed. The residual liver or PEG in the stomach was calculated, using time Vs 100 minus the cumulative percent of fed liver counts or percent PEG recovered each 15 minutes (including 0% recovered at time 0). All the dogs were given the standard meal on at least three occasions prior to pylorectomy and on a minimum of 4 occasions after pylorectomy. Each dog was used as its own control.

Differences between groups were analysed by the Student's t test for unpaired values; differences within dogs were analysed by the Student's t test for paired values. Each point on the graph represents the mean of the observations for all four animals. The observation for each dog was not a single observation, but the mean of at least 3 observations in the control group and 4 observations in the pylorectomy group. The vertical bars in the graphs for the emptying times represent the standard error of the mean. Differences were judged to be significant when $p < 0.05$. In all calculations n was taken as the number of animals ($n = 4$). The relationship between various parameters e.g. antral motility and emptying, was determined by the correlation coefficient (Swinscow, 1979).

ANALYSIS OF RECORDS OF ELECTRICAL ACTIVITY

A technique of cross-correlation analysis was applied to the recordings (Allen et al., 1964). The objective of the method was to determine whether a particular event in one rhythmic sequence is related to a particular event in another cyclically recurring sequence. A consistently well-defined component of one recurring sequence is selected as a reference point and its incidence of occurrence is determined within equal temporal subdivision of the associated cycle of the other recurring phenomena. For this analysis it is essential the waveform continue in well-defined sterotyped form throughout long periods. Recordings were chosen so that definition of all the cycles and reference points would be consistent.

Relationship of antral to duodenal electrical control activity. The maximum negative deflection was selected as the fixed point of reference in each cycle of antral electrical control activity. The maximal positive deflection was selected as the point of reference in each cycle of the duodenal electrical control activity (Figure VI). For simplicity in description of cycles these reference sites were designated as the points of onset of the antral and duodenal electrical control activity.

Two, but more often three or four complete duodenal cycles usually occurred during each antral cycle. For subsequent identification, the duodenal cycle during which an antral cycle started, was

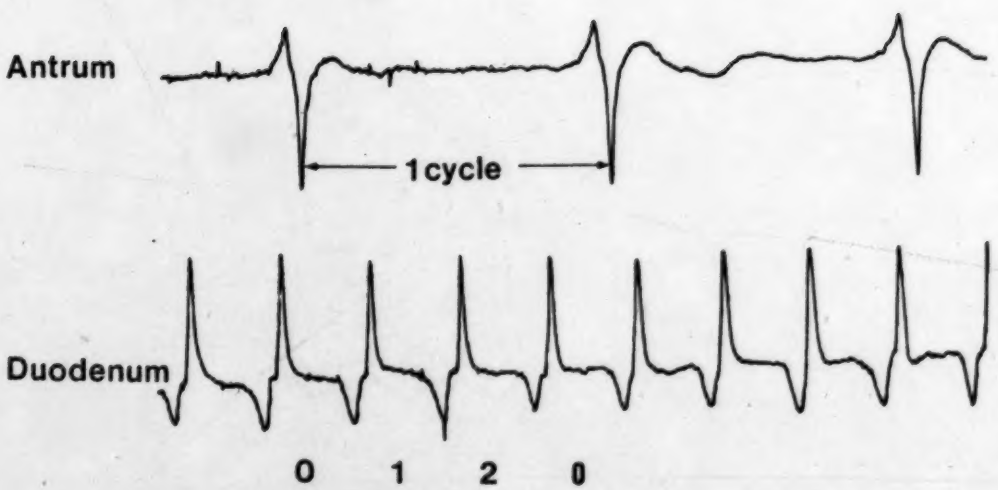

FIG. VI. SIMULTANEOUS RECORDING OF THE ELECTRICAL CONTROL ACTIVITY OF THE ANTRUM AND DUODENUM. THE DUODENAL CYCLE DURING WHICH THE ANTRAL CYCLE STARTED WAS DESIGNATED 0 CYCLE.

labelled 0 and those occurring during the remainder of the antral cycle were numbered in sequence I, II, III and occasionally IV.

To cross correlate antral and duodenal activity, each 0 duodenal cycle was divided into five equal temporal segments (Figure VII). The frequency with which the onset of the antral electrical control activity occurred in each fifth of the 0 duodenal cycle was counted. Mean values for frequency were calculated for each of the dogs.

Incidence of Electrical Response Activity in the Duodenum in relation to the Electrical Control Activity of the Antrum. This analysis was carried out to determine whether a relationship existed between the occurrence of electrical response activity in the duodenum and the time of onset of the antral electrical control activity. Antral cycles were classified as follows: 1) those in which duodenal electrical response activity occurred in duodenal cycle I; 2) those in which duodenal electrical response activity occurred in duodenal cycle II; and 3) those in which no electrical response activity occurred in the associated duodenal cycles. Antral cycles with electrical response activity in duodenal cycle III or IV were rare. The incidence of electrical response activity, in duodenal cycle I when the antral electrical control activity commenced in the first, the second, the third, the fourth and the fifth division of the 0 duodenal cycles, was then determined. The same determinations were made for the incidences

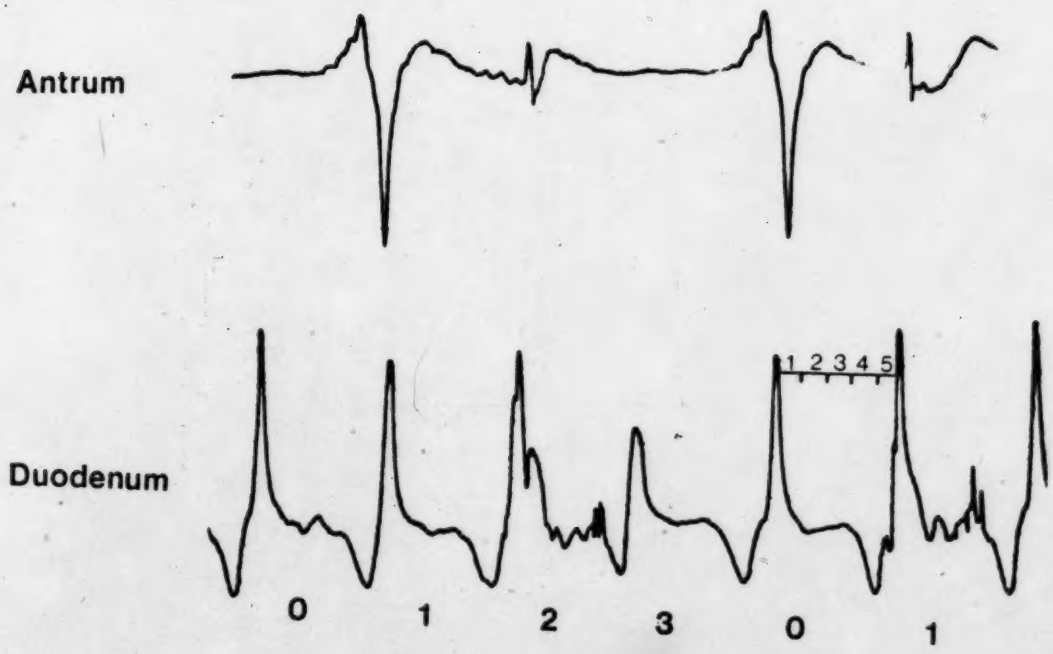

FIG. VII. ELECTRICAL CONTROL ACTIVITY OF ANTRUM AND DUODENUM. O DUODENAL CYCLE HAS BEEN DIVIDED INTO FIFTHS.

of the duodenal electrical response activity in cycle II and for the incidence of duodenal electrical response activity in duodenal cycles III and IV.

Incidence of Antral and Duodenal Electrical Response Activity. Each antral and each duodenal cycle was identified as containing or not containing electrical response activity. The incidences of electrical response activity in the antral cycles and in the duodenal cycles were then calculated separately. Mean values for all of the dogs in the fasted and in the fed state were determined.

ANALYSIS OF CONTRACTILE ACTIVITY

Contractile activity was recorded also for a period of 1 hour before and for a period of 3 hours after feeding. The number of contractions in each 1 minute period was counted and expressed as contractions per minute. A 1 minute motility index was then determined by summing the peak height of all contractions (in millimeters) in each 1 minute period. A 15 minute cumulative motility index was determined by sequentially adding the minute indices for each 15 minute period immediately following feeding in each animal.

INTRALUMINAL PERFUSED PRESSURE RECORDINGS

The pressure changes were recorded by perfused silastic catheters and the height of the pressure waves recorded was measured in mm Hg.

CHAPTER III

RESULTS

Initially 5 dogs were entered in the experiment. One animal (G 293) exhibited persistent tachygastria with antral electrical control activity of 18 - 20/min compared to 4-5/min in the other four "normal" dogs. The findings in this dog will be dealt with separately in Chapter V.

ELECTRICAL ACTIVITY

Relationship of Antral and Duodenal Electrical Control Activity. The antral electrical control activity reference point occurred, with almost equal frequency, in each fifth of the 0 duodenal cycle in fasted and in fed animals, before and after pylorectomy. The number of antral electrical control activity cycles analysed in relation to the 0 duodenal cycle varied in the four dogs but the mean number of cycles analysed for each animal was 200 cycles while fasting, and 600 cycles post-prandially. This procedure was repeated both for controls and following pylorectomy. On analysis of the data no temporal relationship could be demonstrated.

Occurrence of Duodenal Electrical Response Activity in relation to Antral Electrical Control Activity. No relationship was found between the occurrence of electrical response activity in the duodenum and the electrical control activity of the antrum in fasted dogs, either before or after pylorectomy. In each experiment, and in the aggregate tests for each dog, similar values tended to occur in each fifth of the 0 duodenal cycle. In fasted dogs, electrical response activity in the duodenum is independent of the electrical control activity of the antrum.

A marked difference was found with dogs in the post-prandial state. If electrical response activity occurred in duodenal cycle I, the antral reference point tended to be near the beginning of the 0 duodenal cycle (first, second or third temporal segment)(Figure VII). This tendency diminished as the reference point of the antral electrical control activity occurred towards the later portions of the 0 duodenal cycle. As the reference point occurred later in the 0 duodenal cycle, an increasing tendency developed for the electrical response activity to start in duodenal cycle II. This relationship was not evident following excision of the pylorus and these dogs showed, as did the fasted dogs, that electrical response activity in the duodenum is independent of the electrical control activity of the antrum.

Results indicate that, in fed control dogs, electrical response activity in the duodenum is related to the antral electrical control

activity. The electrical response activity does not occur in the duodenal cycle which is simultaneous with the contractions of the antral electrical control activity. It does occur, however, in the next or subsequent duodenal cycles, as the antral electrical control activity starts later in the duodenal sequence.

Antral and Duodenal Electrical Response Activity. Feeding caused a significant increase in the incidence of electrical response activity in the antrum and in the duodenum, both in the controls and following pylorectomy. When the dogs were fasted, 13% of the antral cycles included electrical response activity; after feeding, the incidence increased to 72%. Post-prandially all of the antral cycles showed electrical response activity for long periods (up to 10 minutes) (Figure VIII). The incidence of electrical response activity during fasting was greater in duodenal than in antral cycles, being 32% compared to 13%. On feeding, the duodenal incidence increased to 52%.

Throughout the study each antral cycle spanned 3 to 4 duodenal cycles. The 0 and fourth duodenal cycles rarely contained electrical response activity. When present, the electrical response activity was associated more often with the first and second cycles and sometimes the third cycle. This pattern accounts for the lower incidence of electrical response activity in the duodenal than in the antral cycles in the fed state.

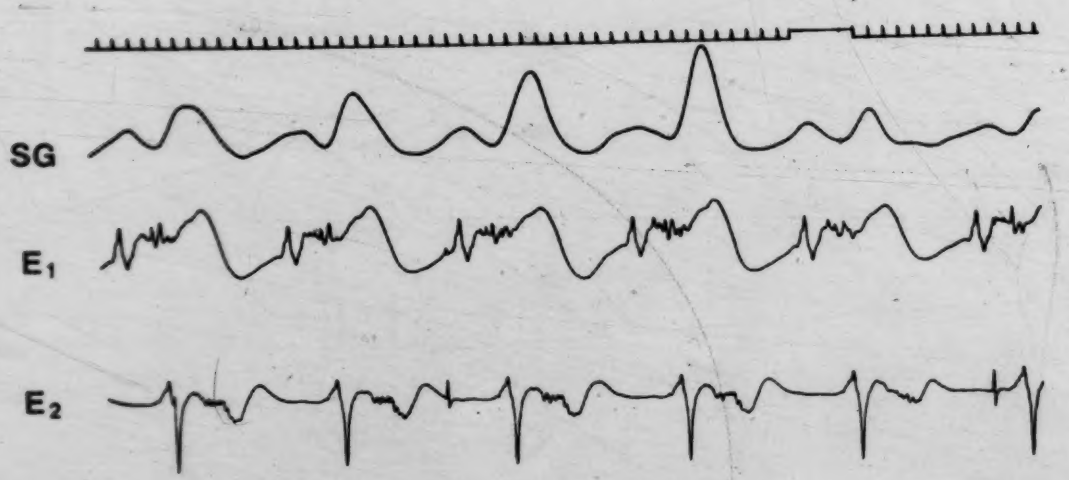

FIG. VIII. ELECTRICAL RESPONSE ACTIVITY ASSOCIATED WITH ALMOST EVERY ELECTRICAL CONTROL ACTIVITY IN THE POST-PRANDIAL PERIOD. TIME MARKER INDICATES SECONDS AND MINUTES.

Feeding increases the electrical response activity in the antrum and in the duodenum, with higher incidence of fast activity in cycles of the electrical control activity of the antrum than those of the duodenum.

Frequency Analysis of Electrical Control Activity of Antrum and Duodenum. A computer frequency analysis was done on antral and duodenal electrical control activity to determine if there was any significant difference during fasting, while feeding and again in the post-prandial period. (Figure IX). The findings of this analysis show that no difference exists between antral and duodenal electrical control activity either before or after pylorectomy, whether the recordings were made while fasting, during feeding, or in the fed state.

Electrical Response Activity during Feeding. Feeding caused inhibition of duodenal electrical response activity and this inhibition was present while the animal was actually eating (Figure X). The electrical response activity returned when the meal was finished. This finding was demonstrated at each meal and in every animal both before and after pylorectomy.

No change in antral electrical response activity was demonstrated during feeding.

	CONTROL		POST PYLORECTOMY	
	ANTRUM	DUODENUM	ANTRUM	DUODENUM
FASTING	5.45	18.35	5.51	18.12
DURING FEEDING	5.39	18.28	5.35	17.81
POST PRANDIAL	5.37	18.52	5.63	17.81

FIG. IX. COMPUTER FREQUENCY ANALYSIS OF ELECTRICAL CONTROL ACTIVITY.

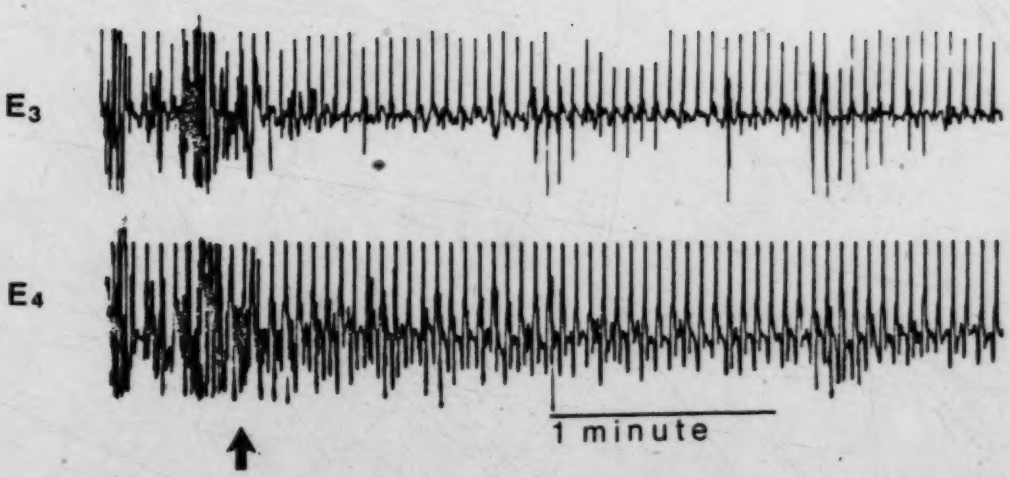

FIG. X. INHIBITION OF DUODENAL ELECTRICAL RESPONSE ACTIVITY DURING FEEDING, INDICATED BY ARROW. INHIBITION CONTINUED FOR RECORDING PERIOD SHOWN.

ANTRAL AND DUODENAL CONTRACTILE ACTIVITY

There was no significant difference in the 15 minute mean cumulative motility index of either the antrum or duodenum, in the controls and post-pylorectomy group (Figure XI and XII). This 15 minute motility index was timed for the first 15 minutes after eating in each dog. No correlation was present, between emptying of solids for the first 15 minutes after feeding and the 15 minute mean antral motility index ($r = 0.91$; $0.1 > p > 0.05$). Following pylorectomy, however, when the same correlation was made the value of p was significant ($r = 0.96$; $0.05 > p > 0.01$). No correlation was found in the control and pylorectomy observations, either between emptying of solids and the duodenal motility index, or between emptying of liquids and the antral or duodenal motility index (r values for these observations varied from 0.04 to 0.83; p value not significant). In calculating the correlation coefficient (r), $n = 4$ and the degree of freedom was therefore $2 (n - 2)$.

INTRALUMINAL PRESSURE

In this experiment intraluminal pressures did not appear to reflect what was occurring in relation to emptying. It certainly did not contribute any further information to that obtained by strain gauges. Indeed, when antral contractile activity was increased, as

CONTROL OBSERVATIONS

	TIME	A	B	C	D	$\bar{x}$
Per-cent of ingested solids emptied each 15 min period	15	17	8	7	11	10.75
	30	21	14	18	22	18.75
	45	30	9	17	4	15
	60	8	1	29	12	12.5
	75	4	10	3	3	5
	90	3	4	1	1	2.25
Per-cent of ingested liquids emptied each 15 min period	15	19	39	36	40	33.5
	30	24	4	23	30	20.25
	45	21	6	5	7	9.75
	60	9	2	7	4	5.5
	75	1	6	1	1	2.25
	90	1	0	0	0	0.25
A.M.I.	0 - 15	2608	2345	2236	2531	2430
D.M.I.	0 - 15	2492	2504	2398	2482	2469

FIG. XI. CONTROL OBSERVATIONS IN ALL FOUR DOGS SHOWING PERCENT OF INGESTED SOLIDS AND LIQUIDS EMPTIED EACH 15 MINUTE PERIOD. FIGURES FOR ANTRAL MOTILITY INDEX (A.M.I.) AND DUODENAL MOTILITY INDEX (D.M.I.) ARE ALSO SHOWN. $\bar{X}$ = MEAN VALUES

POST-PYLORECTOMY OBSERVATIONS

	TIME	A	B	C	D	$\bar{X}$
Per-cent of ingested solids emptied each 15 min period	15	14	0	6	2	5.5
	30	45	1	11	12	17
	45	12	2	8	5	6.75
	60	11	23	12	1	11.75
	75	3	15	7	5	7.5
	90	3	9	6	9	6.75
Per-cent of ingested liquids emptied each 15 min period	15	59	4	13	16	23
	30	20	4	26	29	19.75
	45	3	7	23	30	15.75
	60	1	6	4	4	3.75
	75	1	14	3	2	5
	90	0	13	3	3	4.75
A.M.I.	0 - 15	2203	651	1727	987	1392
D.M.I.	0 - 15	2113	2507	1997	2169	2084

FIG. XII. POST-PYLORECTOMY OBSERVATIONS IN ALL FOUR DOGS SHOWING PERCENT OF INGESTED SOLIDS AND LIQUIDS EMPTIED EACH 15 MINUTE PERIOD. FIGURES FOR ANTRAL MOTILITY INDEX (A.M.I.) AND DUODENAL MOTILITY INDEX (D.M.I.) ARE ALSO SHOWN.
$\bar{X}$ = MEAN VALUES

shown by the strain gauges, the pressures obtained by the intraluminal tubes were often low (10 - 15 mm Hg). A high pressure zone was not recorded at the gastro-duodenal junction. The pressure changes recorded in the controls reflected closely the antral pressure waves. Following pylorectomy no pressure was recorded in this area, showing that there was very little, if any, contraction occurring in the region of the anastomosis.

EMPTYING OF STANDARD MEALS

The blenderized dog food and liver fed were sized on sieves, and feeds were of uniform particle size, passing through a sieve of 3 mm pore size.

In the standard feeding experiments all of the dogs took both the water and solid food offered. The percent of PEG recovered was 75% while that of ^{99m}Tc was 78% - however, in a number of experiments up to 99% of PEG was recovered and up to 96% of ^{99m}Tc, indicating adequacy of the fistula and collection methods for recovery of fed materials.

Emptying of Liquids Vs Solids. In the control and pylorectomy observations (n = 4) although the liquids were apparently emptying

faster than solids, there was no statistical significance between the emptying rates (Figure XIII and XIV).

Emptying of Liquids. The volume of liquid given was varied from 100 ml to 600 ml (n = 4) but there was no statistically significant difference between the amounts recovered or the time taken to empty in both groups. However, as the volume given increased, the emptying rate increased, but again there was no statistical difference between the percent of the total feed emptied during each 15 minute period.

The curve for emptying of liquids in all animals could be divided into three phases; a slow initial emptying period for the first 15 minutes, a faster emptying period from 15 to 60 minutes, followed by a slow period after 60 minutes (Figure XV).

Emptying of Solids. The weight of liver varied from chicken to chicken, the mean being 40 G (± 10.8). This was mixed with 100 G of canned dog food (Dr. Ballards) and then blenderized. The food particle size obtained was standard, passing through a sieve of 3 mm. The emptying rate of solids was not significantly slower following pylorectomy (Figure XVI). No difference was present in the emptying rate of solids when given with varying volumes of liquids.

The curve for emptying of solids could again be divided into 3 phases: a) a slower initial 15 minute emptying, b) a faster emptying phase from 15 to 60 minutes and, c) a third slower phase.

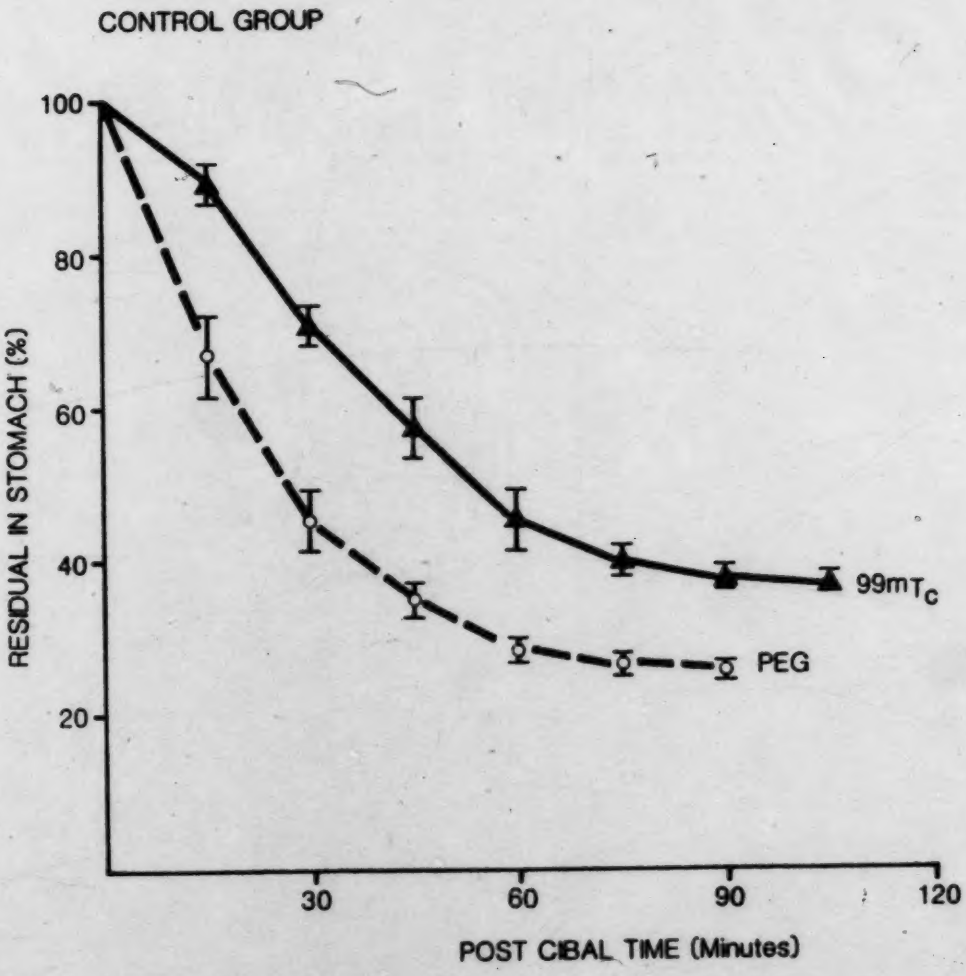

FIG. XIII. EMPTYING OF LIQUID VS SOLIDS IN CONTROL GROUP (n = 4).

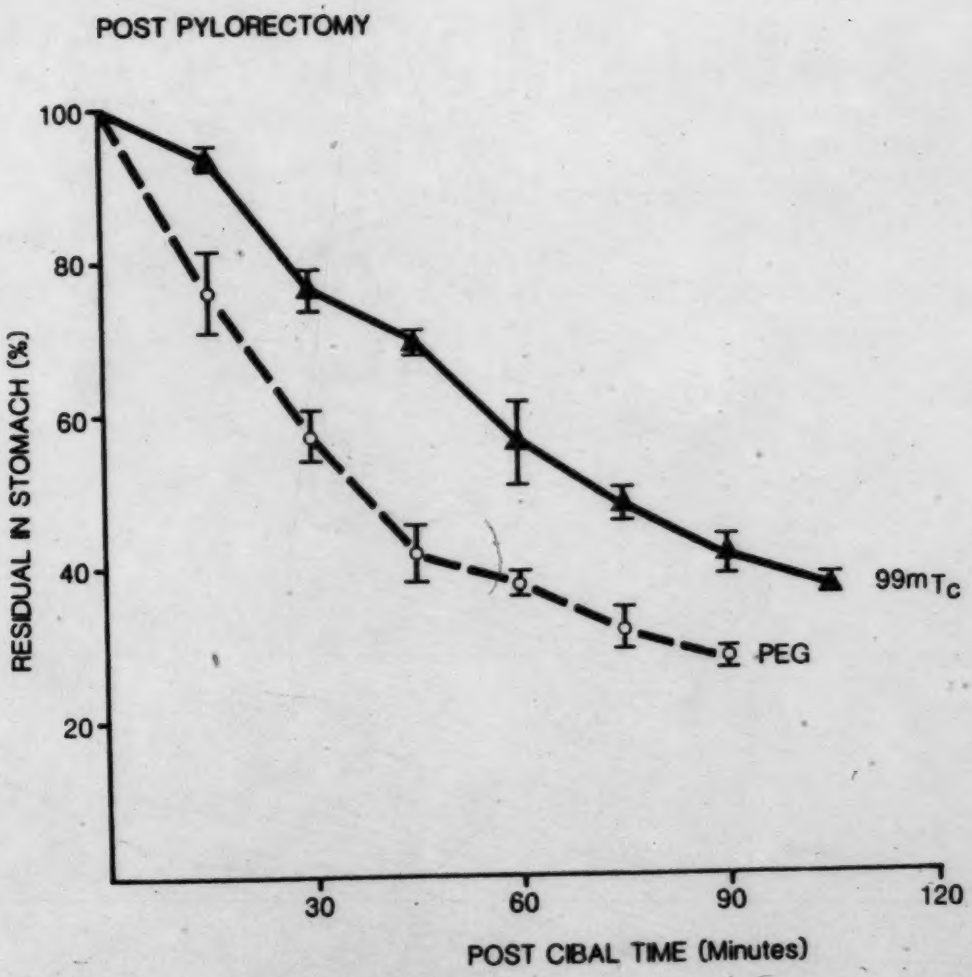

FIG. XIV. EMPTYING OF LIQUIDS VS SOLIDS IN POST-PYLORECTOMY GROUP (n = 4).

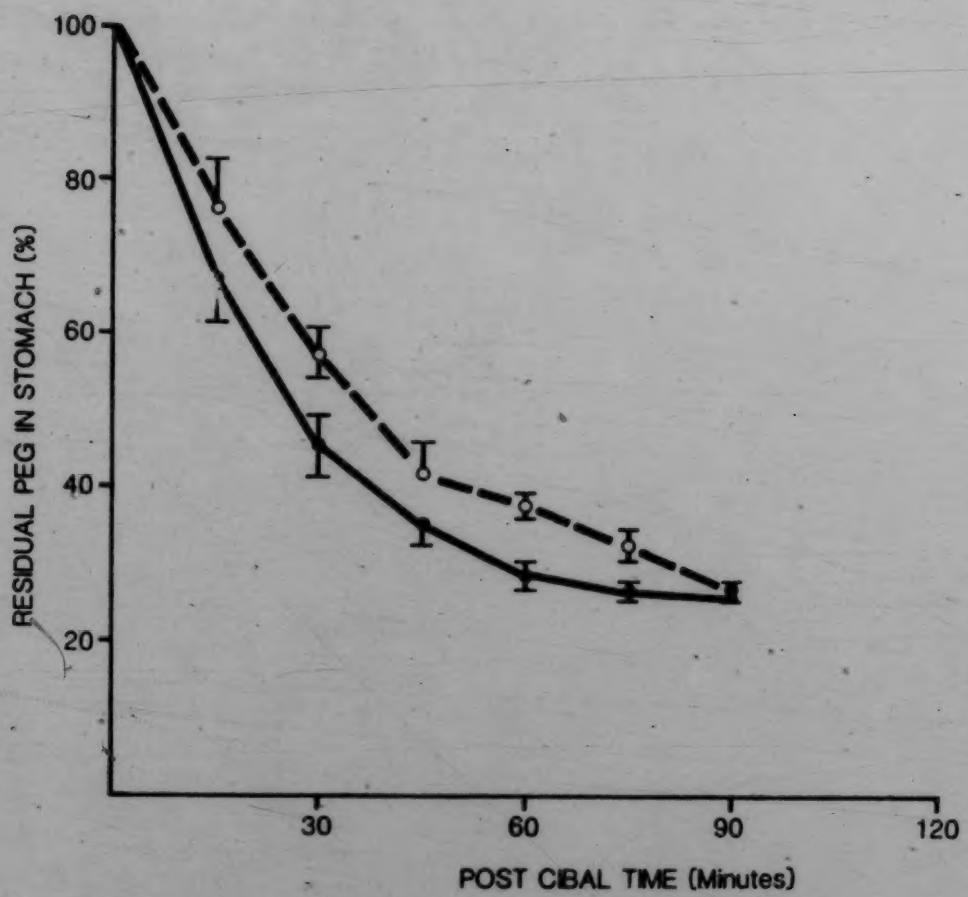

FIG. XV. RESIDUAL PEG IN STOMACH
●——● CONTROLS (n = 4).
o---------o POST-PYLORECTOMY (n = 4).

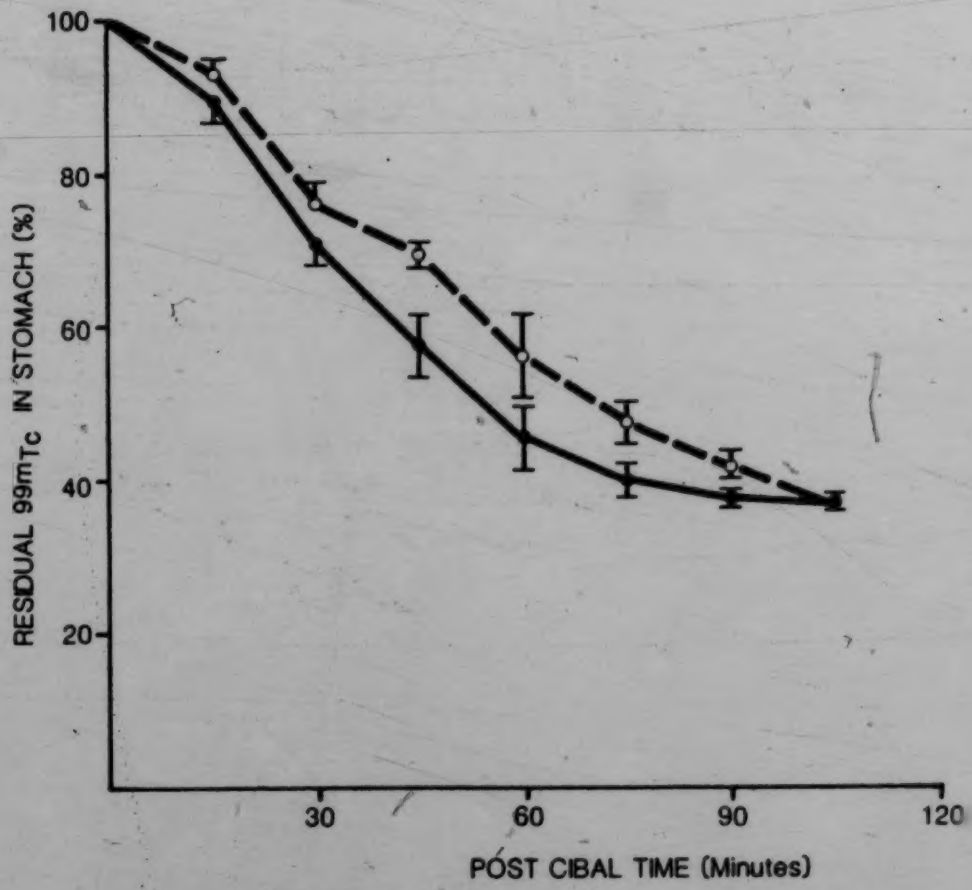

FIG. XVI. RESIDUAL ^{99m}Tc IN STOMACH
●——————● CONTROLS (n = 4).
o---------o POST-PYLORECTOMY (n = 4).

MIGRATING MYOELECTRIC COMPLEX (MMC)

Any MMC seen was noted and intervals measured and compared to standard published parameters of normal MMC in un-cannulated dogs (Code and Marlett, 1974). This was to ascertain whether the presence of the cannula in the duodenum affected motility.

A total of 9 MMC was observed in the stomach and duodenum of each of the four dogs studied prior to pylorectomy. In every instance in the controls, the gastric antrum developed the same cyclic recurrent sequence of electrical response activity as the duodenum. Practically each phase of every cycle was present simultaneously in the stomach and the duodenum. The termination of the activity front, that is, the end of the period of intense electrical response activity, was the most sharply defined interphase. It occurred simultaneously in the stomach and duodenum. Thus, in normal dogs, the interdigestive myoelectric complexes of the stomach and duodenum are locked together in a nearly simultaneous relationship.

Phases of each cycle of complex in normal dogs. Phase I of the interdigestive complex was characterized in both the antrum (Figure XVII) and the duodenum (Figure XVIII) by relative absence of electrical response activity compared to the other phases.

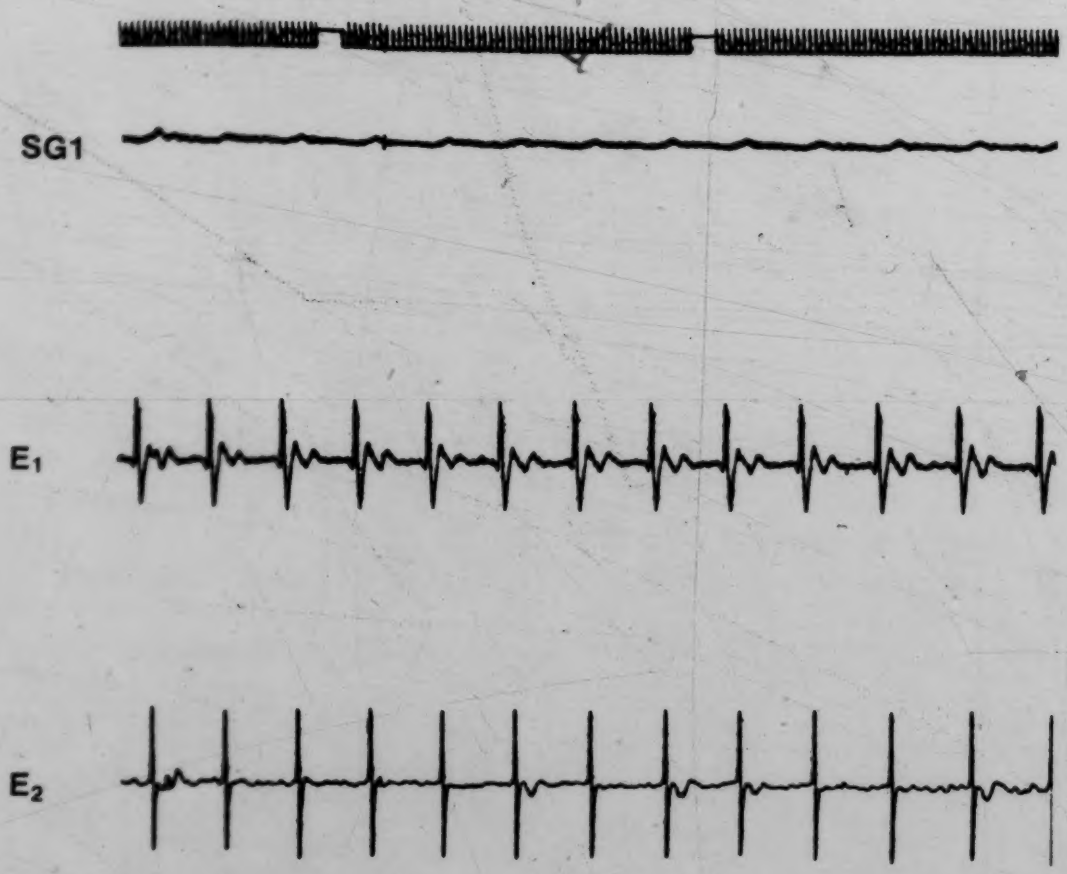

FIG. XVII. PHASE I OF ANTRAL MIGRATING MYOELECTRIC COMPLEX (MMC). < 10% OF ELECTRICAL CONTROL ACTIVITY WITH ELECTRICAL RESPONSE ACTIVITY. S.G.I. ANTRAL STRAIN GAUGE; E_1 AND E_2, ANTRAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

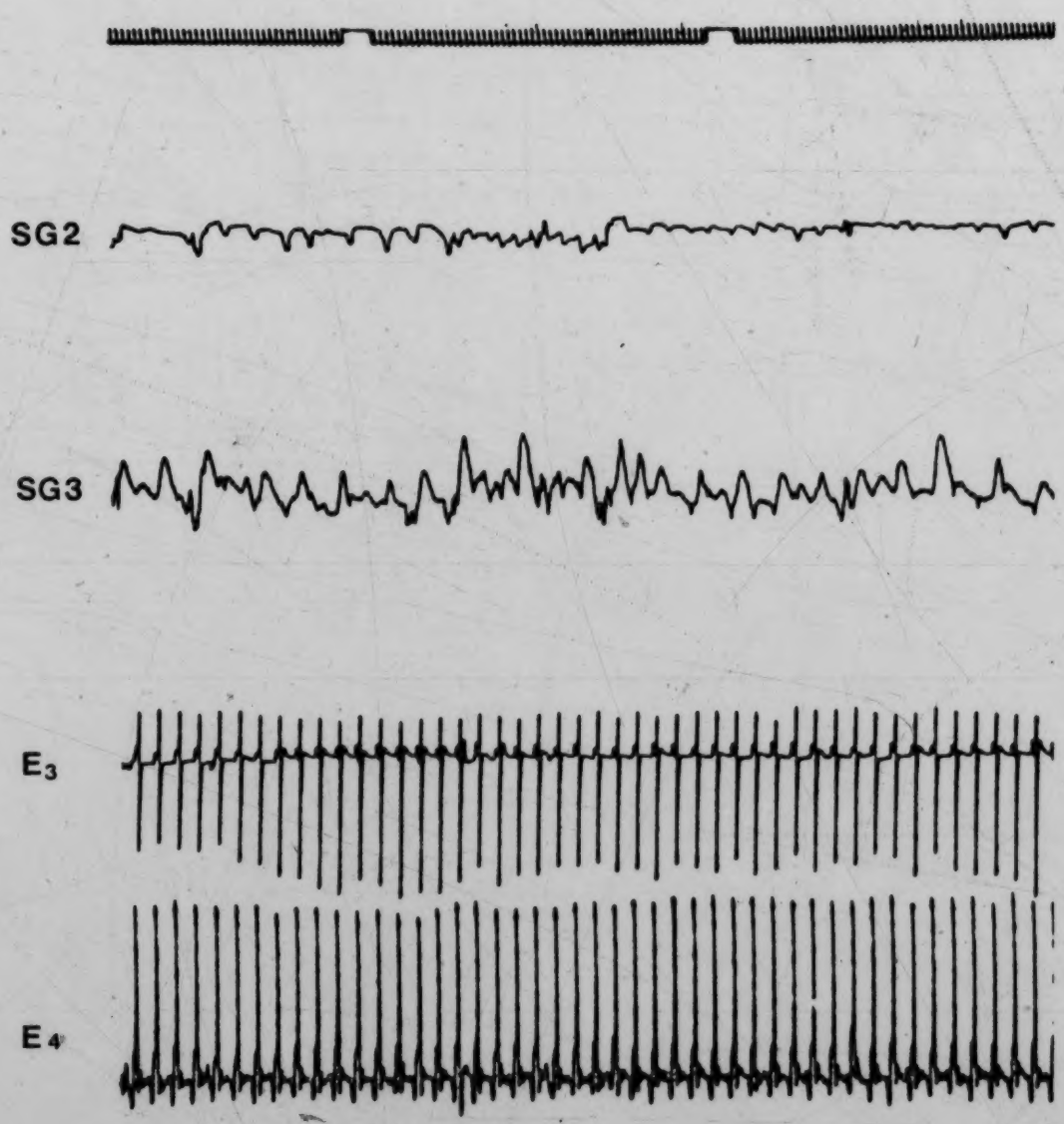

FIG. XVIII. PHASE I OF DUODENAL MMC. < 10% OF ELECTRICAL CONTROL ACTIVITY WITH ELECTRICAL RESPONSE ACTIVITY. S.G. 2 AND S.G. 3 - DUODENAL STRAIN GAUGES E_3 AND E_4 - DUODENAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

Phase II was identified as the first 3 minutes of recording with electrical response activity was associated with at least 10% of the electrical control activity (Figure XIX and XX).

Phase III was characterized by the sudden onset and continuous occurrence of bursts of electrical response activity with every electrical control activity (Figure XXI and XXII). The end of phase III was almost as sudden as its beginning.

Phase IV was characterized by a rapid decrease in incidence and a rapid decrease in intensity of electrical response activity (Figure XXIII and XXIV). It was considered over as soon as 3 minutes of recording had less than a 10% incidence of electrical response activity.

In the controls, the mean duration of the MMC in both antrum and duodenum was (Figure XXV) similar to that found by other workers (Code and Marlett, 1974).

MMC Following Pylorectomy. The MMC in the duodenum, following pylorectomy, showed no change from the controls in either duration, or frequency.

The antral recordings, following pylorectomy, in the fasted dog did not show a normal MMC pattern and the four phases were not present. The antrum showed antral arrythmia (Figure XXVI) which in 82% of the recordings coincided with phase III of the MMC in the duodenum. This arrythmia in the remaining 18% of the recordings was associated with phase I of the MMC in the duodenum.

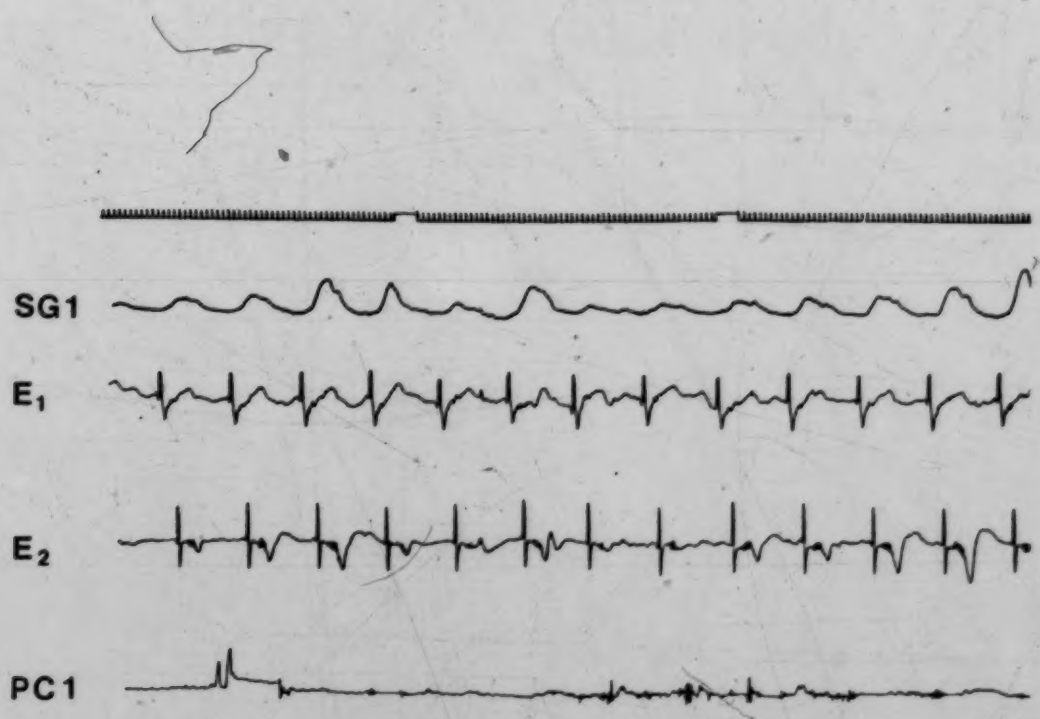

FIG. XIX. PHASE II OF ANTRAL MMC. > 10% OF ELECTRICAL CONTROL ACTIVITY WITH ELECTRICAL RESPONSE ACTIVITY. S.G. 1 - ANTRAL STRAIN GAUGES; E_1 AND E_2 - ANTRAL ELECTRODES; P.C.I - PERFUSION CATHETER. TIME MARKER INDICATES SECONDS AND MINUTES.

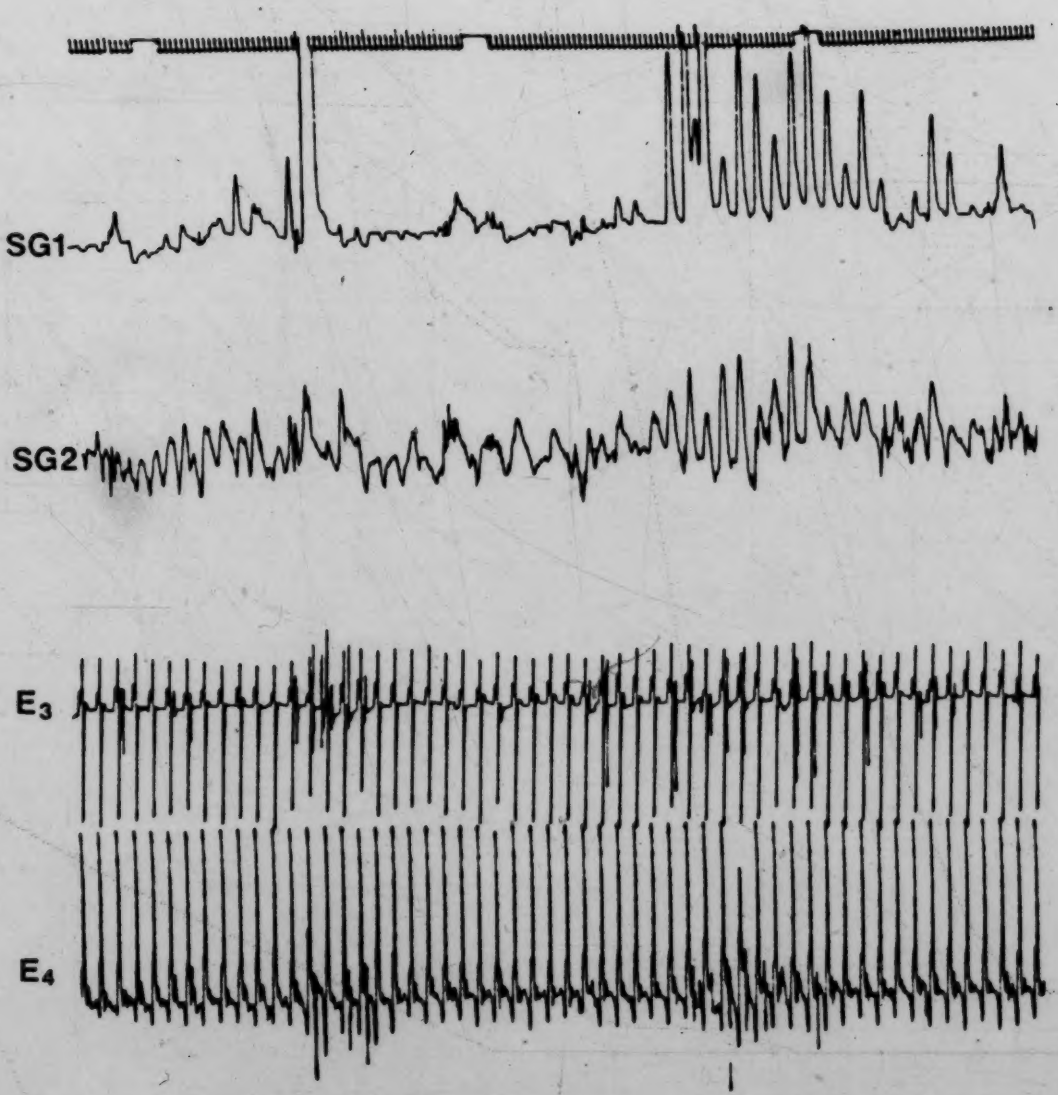

FIG. XX. PHASE II OF DUODENAL MMC. > 10% OF ELECTRICAL CONTROL ACTIVITY WITH ELECTRICAL RESPONSE ACTIVITY. S.G. 1 AND S.G. 2 - DUODENAL STRAIN GAUGES; E_3 AND E_4 - DUODENAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

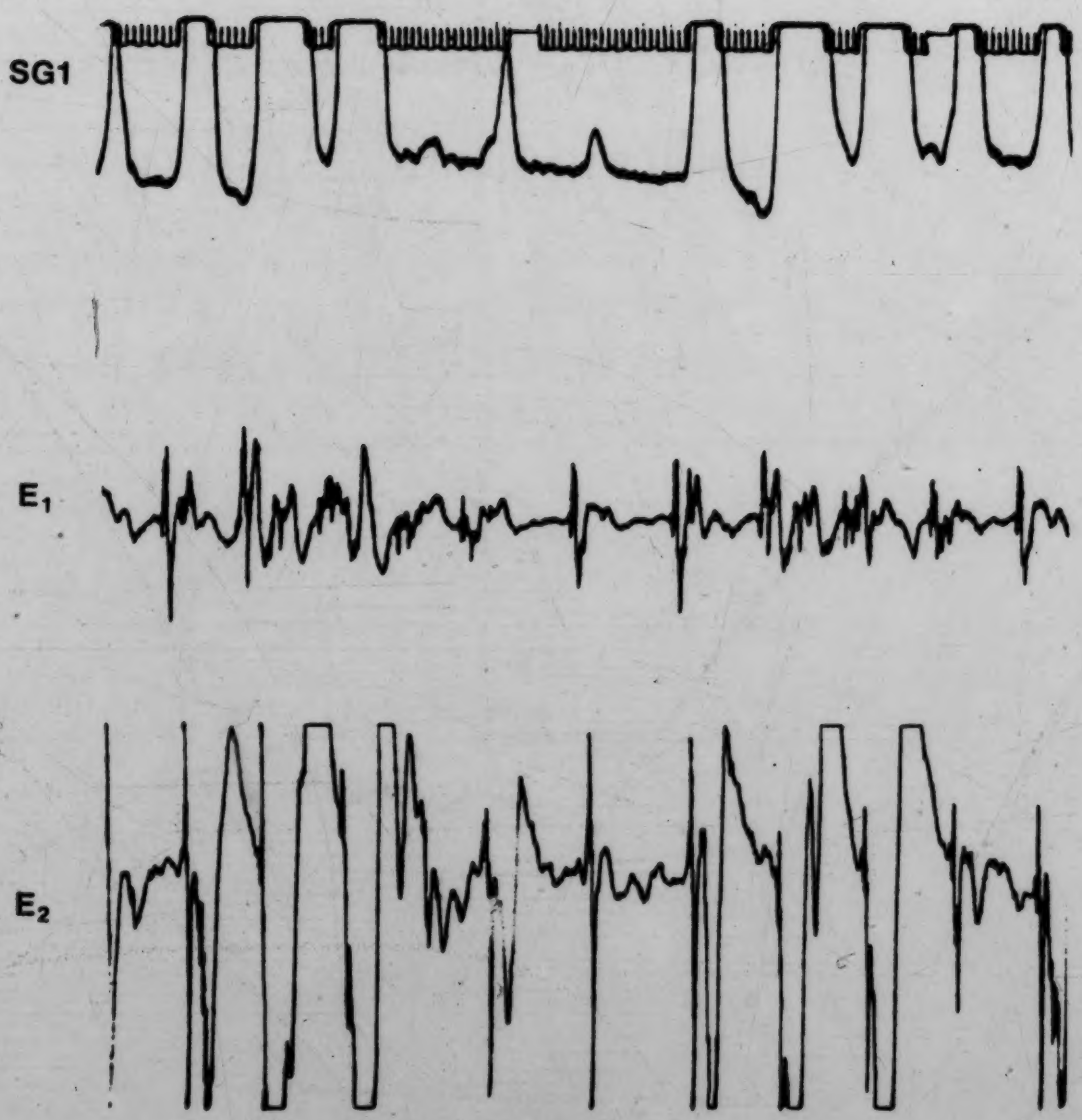

FIG. XXI. PHASE III OF ANTRAL MMC. CONTINUOUS OCCURRENCE OF LARGE ELECTRICAL RESPONSE ACTIVITY WITH EACH ELECTRICAL CONTROL ACTIVITY. S.G. 1 - ANTRAL STRAIN GAUGE; E_1 AND E_2 - ANTRAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

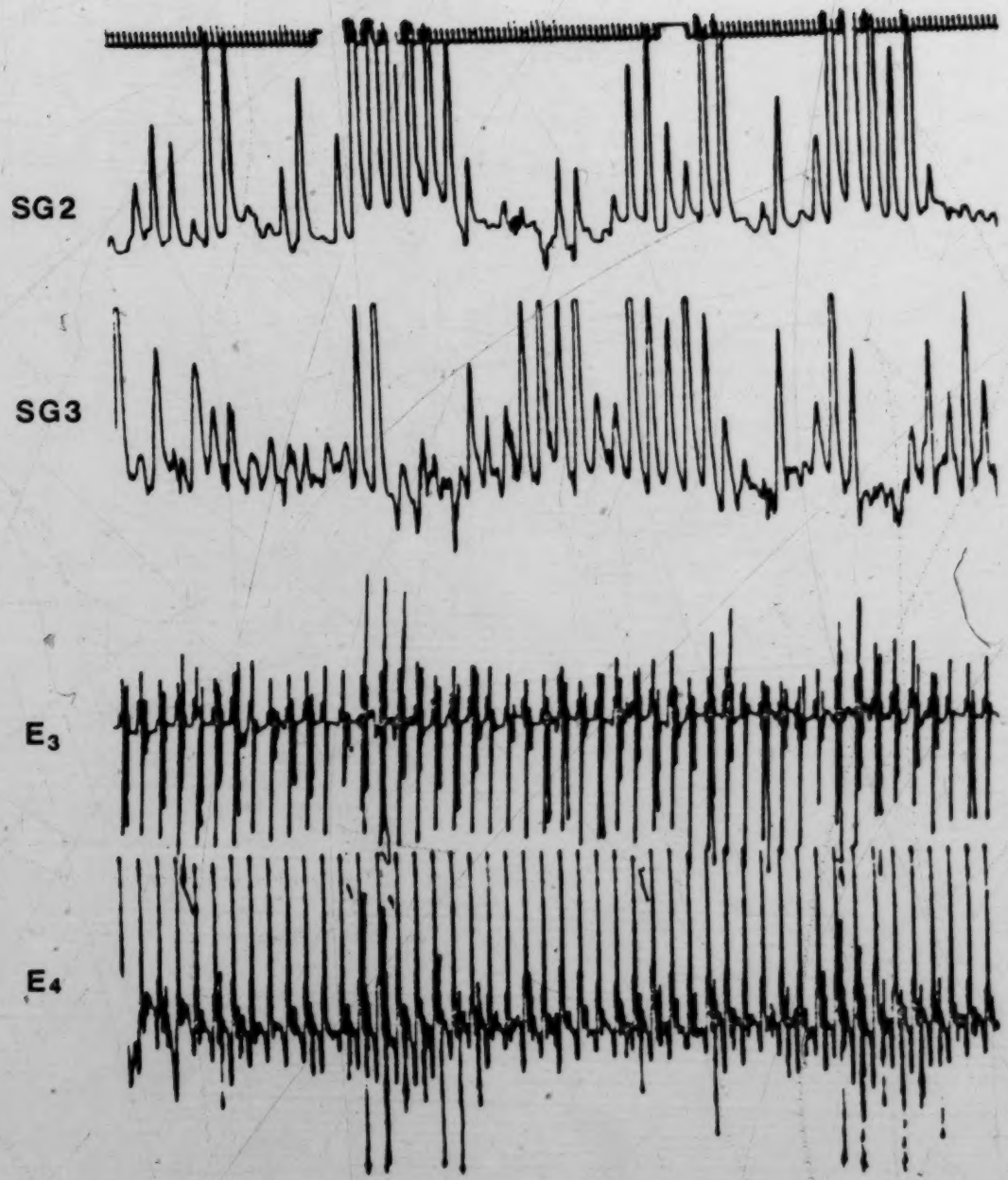

FIG. XXII. PHASE III OF DUODENAL MMC. CONTINUOUS OCCURRENCE OF LARGE ELECTRICAL RESPONSE ACTIVITY WITH EACH ELECTRICAL CONTROL ACTIVITY. S.G. 2 AND S.G. 3 - DUODENAL STRAIN GAUGES; E_3 AND E_4 - DUODENAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

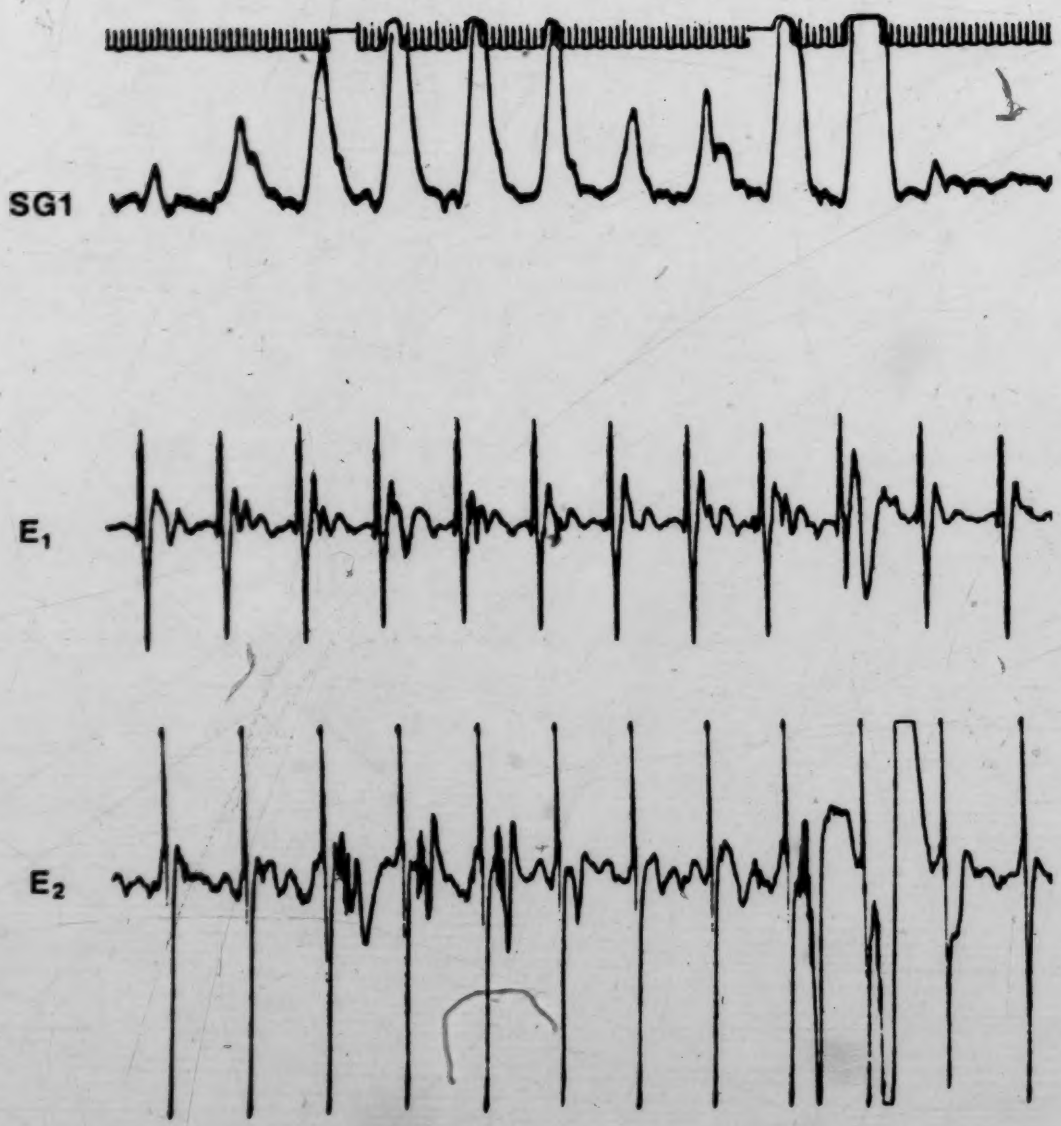

FIG. XXIII. PHASE IV OF ANTRAL MMC. RAPID DECREASE IN INCIDENCE AND INTENSITY OF ELECTRICAL RESPONSE ACTIVITY, S.G. 1 - ANTRAL STRAIN GAUGE; E_1 AND E_2 - ANTRAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

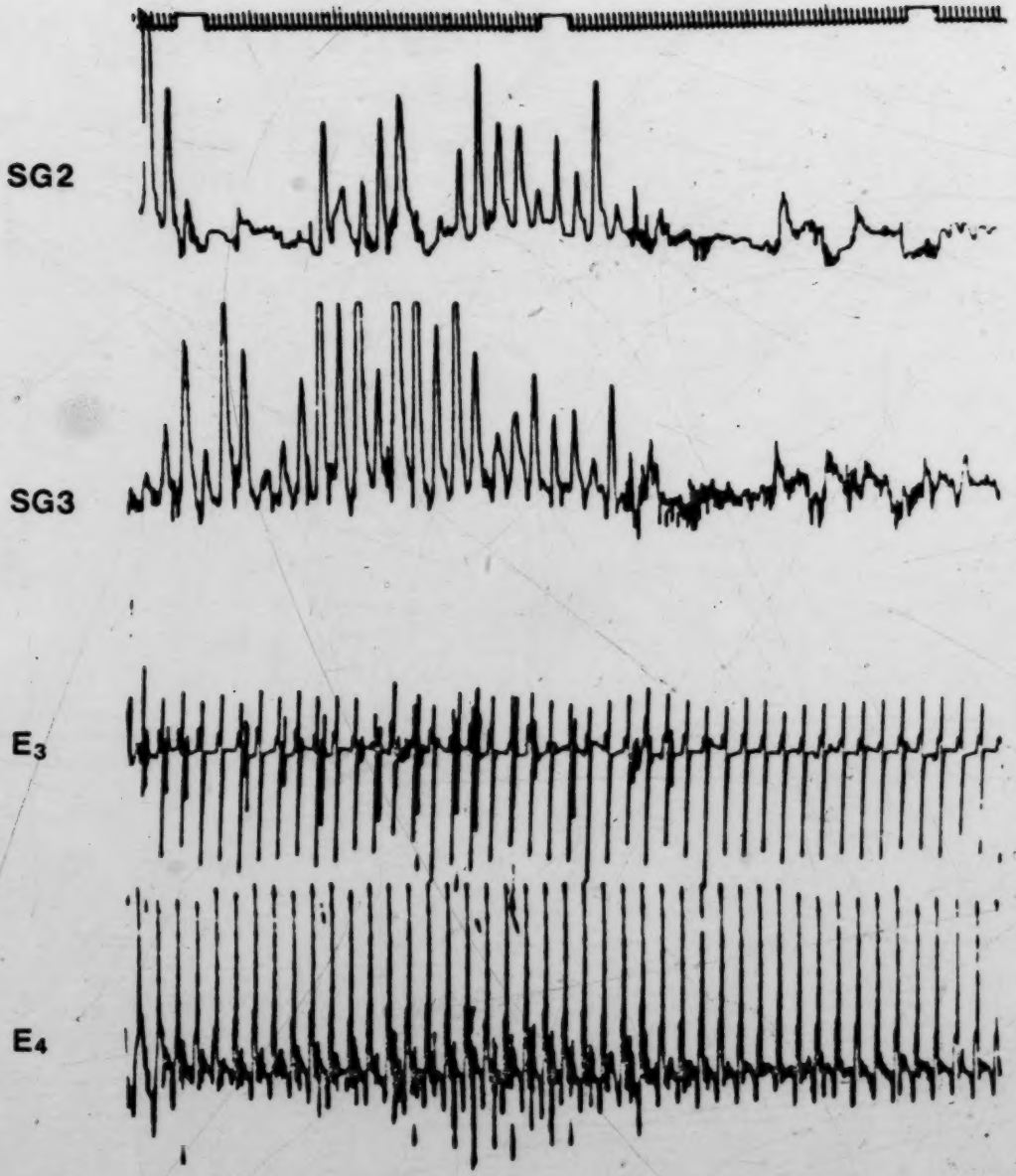

FIG. XXIV. PHASE IV OF DUODENAL MMC. RAPID DECREASE IN INCIDENCE AND INTENSITY OF ELECTRICAL RESPONSE ACTIVITY. S.G. 1 AND S.G. 2 - DUODENAL STRAIN GAUGES; E_3 AND E_4 - DUODENAL ELECTRODES.

	ANTRUM (n = 4)	DUODENUM (n = 4)
PHASE I	39	34
PHASE II	31	28
PHASE III	12	7
PHASE IV	8	9

FIG. XXV. MEAN TIME IN MINUTES OF EACH PHASE OF MIGRATING MYOELECTRIC COMPLEX RECORDED IN CONTROLS.

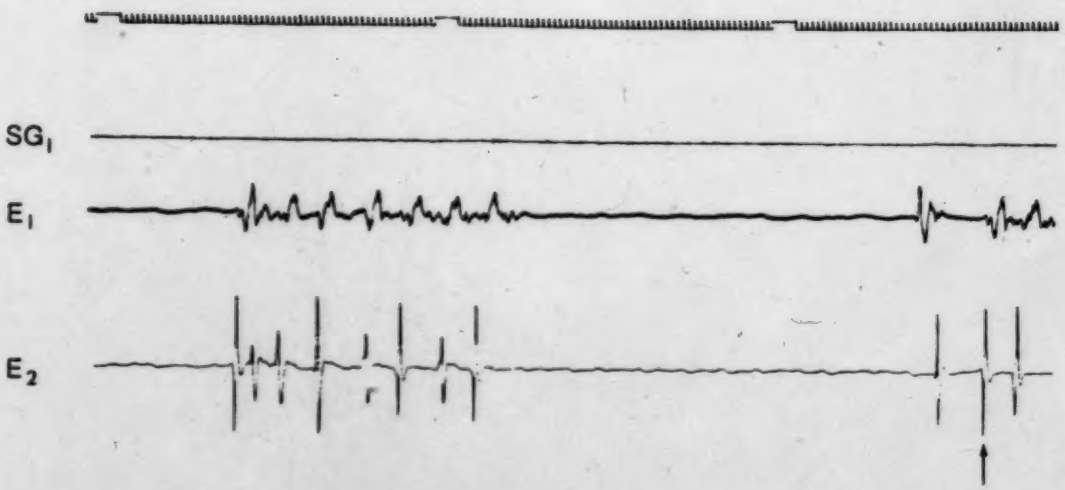

FIG XXVI. ANTRAL ARRYTHMIA FOLLOWING PYLORECTOMY AND IN THE FASTED STATE, SHOWING REVERSAL OF POLARITY (↑) AND COMPENSATORY PAUSE.

During this antral arrythmia the polarity of the electrical waveform changed from positive-negative to negative-postive (Figure XXVI). Orad propagation of the antral electrical control activity also occurred (Figure XXVII). The antral frequency, when this occurred, increased to 7-8 cycles/minute (normal 4-5 cycles/minute). These bursts of antral arrythmia were then followed by a compensatory pause, often lasting as long as 80 seconds.

POST-MORTEM FINDINGS

A post-mortem examination was performed on all animals after completion of the entire battery of planned tests. There was no morbidity or mortality associated with this study. After sacrificing the animals, various degrees of omental and liver adhesions to the implanted devices and adjacent gastroduodenal serosa were seen. There was no evidence of any intra-abdominal peritonitis, abcess formation or leaks from either the anastomotic site or the site of implantation of the cannula. The site of the gastro-duodenal anastomosis was patent with no evidence of stricture formation.

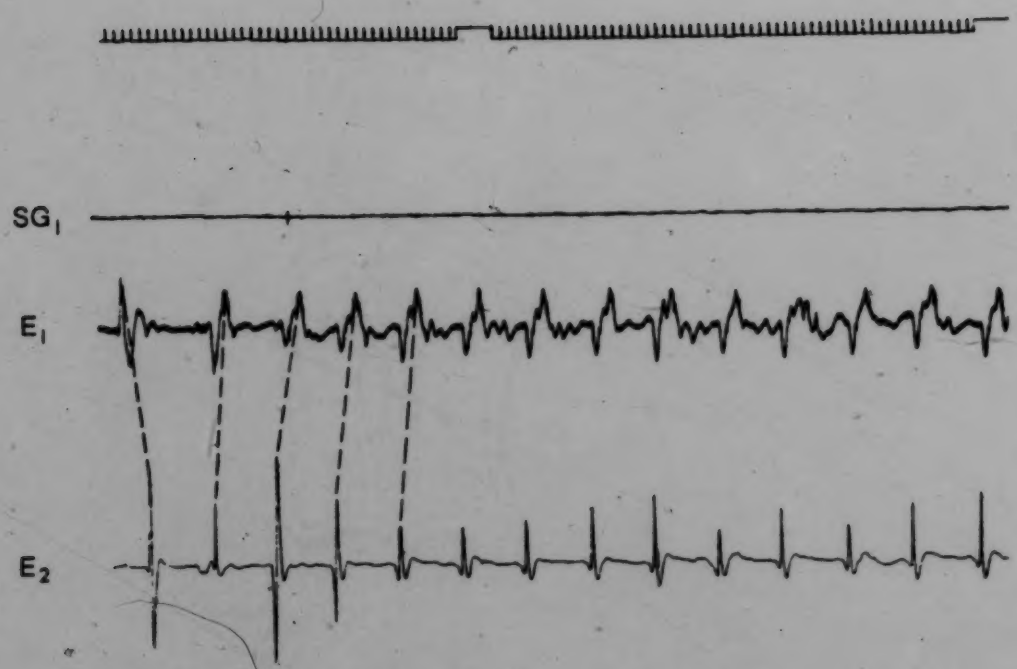

FIG. XXVII. ANTRAL ARRYTHMIA SHOWING ORAD PROPAGATION. S.G.1 - ANTRAL STRAIN GAUGE; E_1 AND E_2 - ANTRAL ELECTRODES. TIME MARKER INDICATES SECONDS AND MINUTES.

CHAPTER IV

DISCUSSION

The results of this study indicate that removal of the pylorus leads to loss of antro-duodenal co-ordination in the post-prandial period, as judged by recordings of myogenic electrical activity and gastroduodenal contractions. However, pylorectomy did not appear to affect rates of gastric emptying of solids and liquids. Each of these observations will now be discussed in detail.

Myogenic Electrical Activity. In this study there was no temporal relationship between electrical activity in the antrum and duodenum during periods of fasting. A temporal relationship was present immediately after meals, indicating that antro-duodenal co-ordination occurred at this time. This agrees with the findings of Allen et al., (1964). Antro-duodenal co-ordination was absent following pylorectomy. Similar results were reported by other workers who transected the gastroduodenal junction (Bedi and Code, 1972; Atanassova, 1969). Transit of food into the duodenum, which will be discussed later, was not affected by pylorectomy. Some other factor which initiates co-ordination must be present. Sarna and Daniel (1976) have shown that antro-duodenal co-ordination is

present through the myenteric nerve plexus. By excision of the pylorus this neural mechanism is destroyed and thus the antro - duodenal co-ordination is lost.

Bass et al., (1978) have suggested that following excision of the duodenal bulb in dogs the duodenal electrical control activity was decreased by 2-3/minutes. On a computer frequency analysis of all our animals, both before and after pylorectomy, no statistical difference was observed. Mean figures were computed for both antrum and duodenum while fasting, during feeding, and in the post-prandial period. The results show that the frequency of the duodenal electrical control activity has no temporal relationship to the antral electrical control activity and indeed appears to be independent of it.

During actual feeding by the animals no duodenal electrical response activity was observed. This phenomenon, which has not been previously described, was observed in all the animals both prior to and following pylorectomy. There is no clear explanation for this duodenal inhibition during feeding. It may be mediated by extrinsic vagal fibres to the coeliac plexus and from there by fibres to the duodenum. Excitatory vagal nerves do go from coeliac plexus to duodenum but inhibitory fibres must also be present.

Contractile Activity. Although the method of measurement of contractile activity is relatively crude, it is still one of the best

methods available. Comparison between animals is difficult, because the precalibrated strain gauge transducers cannot be accurately recalibrated after implantation. Although accurate prior to implantation, operative suturing of the gauges to the gastric and duodenal walls, and gradual development of adhesions to the gauges during the study period, preclude the reliance on the original calibration. The actual amplitude values have no real meaning. However, by measuring in each dog the 1 minute motility index, (height of contractions in mm. X frequency of contractions per minute), comparision of pattern changes obtained seem justified.

In this investigation the only significant correlation present between the 15 minute antral motility index and emptying of solids was in the pylorectomy groups. However, in the control animals the p value for the correlation coefficient factor ($r = 0.91$) certainly approached a significant value ($0.1 > p > 0.05$). This was for a sample of 4 with a degree of freedom of only 2. If the same trend, as observed, was to continue and more animals were studied, the data obtained would possibly then be significant. The interpretation of the relationship between antral motility and gastric emptying of solids in this study suggests that solids empty from the stomach when the antrum is contracting, and that the duodenum plays little, if any, part in the inhibition of gastric emptying. These findings agree with other published works (Weisbrodt et al., 1969; Stemper and Cooke, 1975).

Because of the very nature of the experimental design, it was not possible to study large numbers of animals. Indeed the aim was an intense study of a small number over a long period. The sample size (n = 4) is consequently small and it is difficult to show significant differences when a statistical analysis is applied.

Intraluminal Pressure. It should be noted that intraluminal pressure is recorded via perfused catheters. The outflow from these is affected not only by the intraluminal pressure within the segment of the organ adjacent to the tip of the catheter, but is also affected by contact between the catheter tip and the wall of the organ (e.g. when the organ contracts). Therefore, a multiple perfused catheter system gives an indication of motor activity but does not give a valid indication of gradients of pressure at two sites (e.g. stomach and duodenum).

Contrary to the findings of Fisher and Cohen (1973), a higher pressure zone was not recorded at the gastroduodenal junction. The pressure changes recorded in the controls reflected closely the antral pressure waves. The exact position of the perfusion catheters was determined at their implantation during operation. They were subsequently sutured in place. Therefore, only one clear explanation exists for the pressure recorded in the pylorus. It is probable in the dog, if not in man, that the pyloric ring is not a tonically

contracted sphincter, opening occasionally, but that it behaves as the distal end of the thickened muscle mass surrounding the antrum and is part of that single muscle unit.

Following pylorectomy the pressure recorded was zero, showing that there were very few, if any, contractions occurring in the region of the anastomosis.

Gastric Emptying of Solids and Liquids. The method of radio-labelling the liver was described by Meyer et al., (1979). They have shown, that ^{99m}Tc in liver reflects the behavior of the liver mass over a wide range of digestion, and that the liver is uniformly labelled with ^{99m}Tc. These findings were confirmed in this experiment and indeed the coefficient of variation of specific activity among samples from any one liver ranged from 9% to 16%. The labelling of water with PEG has been shown to be a very accurate method for determining the liquid phase of gastric emptying (Malawer and Powell, 1967). In this study, the percentage of PEG recovered was 75% while that of ^{99m}Tc was 78%. However, in a number of experiments up to 99% of PEG was recovered and up to 96% of ^{99m}Tc, indicating adequacy of the fistula and collection methods for recovery of fed materials. Assay of the marker concentrations enables the volume remaining in the stomach at each sampling time to be calculated, permitting determination of the emptying rate. However, no measurement of

gastric secretion is obtained when using mixed meals of solids and liquids and, therefore, the test measures emptying of the gastric contents, not emptying of the test meal (Heading, 1980). If the volume of the gastric juices, which were secreted, was required, a second cannula would have to be inserted into the stomach; sampling of the gastric contents could then be made at fixed intervals. The volume of gastric secretion could be estimated by this method. The presence, however, of a cannula in the stomach could possibly interfere with normal gastric motility and for this reason it was omitted.

Although liquids apparently emptied faster than solids in all of the animals, in both the control and pylorectomy observations, these findings were not statistically significant. Again, prior to and following pylorectomy, no difference was shown in the emptying rates for solids. Even when the volume of liquids given with the mixed meals was varied from 100 ml to 600 ml, the emptying rates for solids remained the same.

The method used, in presenting the data on emptying rates in this study, I believe to be a more accurate reflection of the pattern of gastric emptying than the method suggested by Hunt and Spurrell (1951), and by Hopkins (1966). Both the emptying rates for solids and liquids were plotted, as suggested by them, as either the logarithm or square root relation versus time. A linear relationship

for volume versus time could be plotted for the first 60 minutes. This method does not fit for emptying after 60 minutes when the volume in the stomach becomes smaller. This is simply a method for resolution of the data and does not, I believe, reflect the emptying pattern seen. Given the number of variables and their determinants it is questionable whether a simple relationship could be expected.

Clearly, the emptying of a mixed solid and liquid meal is obviously a very complex system. Solids empty more slowly than accompanying liquids until they have been milled by antral activity to a homogeneous mixture; then they are entrained with the liquid. There must, therefore, be a different set of control mechanisms for solids. The extent to which they are independent of the control set for emptying of liquids is unclear. Volume of liquids apparently does not affect emptying of solids. Removal of the pylorus does not affect significantly the rate of emptying of liquids or solids. Indeed, the interpretation of the data in this study suggests no unique function for the pylorus. It would seem that the pylorus should be regarded simply as the distal part of the gastric antrum.

Migrating Myoelectric Complexes. A new finding in this study was that a normal antral MMC did not occur following excision of the pylorus. Antral arrythmia, with reversal of polarity of the electrical waveform, was noted in the fasted, post-pylorectomy

animals. The antral frequency during these periods increased to 7-8 cycles/minute. Orad propagation of the antral electrical control activity also occurred. These bursts of activity were then followed by a compensatory pause, often lasting as long as 80 seconds. The MMC of the stomach and duodenum are locked together in a nearly simultaneous relationship (Code and Marlett, 1974). By excising the pylorus, this relationship is lost and indeed normal MMC does not occur in the antrum. This suggests a feedback myoneural mechanism from the duodenum which, not only initiates the antral MMC, but also controls the frequency. No clear explanation exists for the reversal of polarity which occurred.

Since a study of the MMC in animals was not the primary aim of this project, only one dog was studied in the fasting state for any length of time following pylorectomy. This dog was studied approximately 4-5 hours daily during a 6 week period, while the other animals were studied for only a two week period. However, none of these animals exhibited a normal antral MMC following removal of the pylorus. This finding certainly merits further and more intensive investigation.

Clinical Aspects of Study. Finally, this data may have direct clinical relevance to the gastric emptying patterns seen after surgery, since rapid emptying has been thought to be a major factor

in the production of postoperative dumping and diarrhoea. Confusion has been introduced by conflicting findings arising from application of different methods of study and in particular, by the failure of many investigators using isotope methods to pay sufficient attention to the early phase of emptying (Heading, 1980).

The interpretation of the data in this study suggests that in order to maintain a normal gastric emptying pattern for solids the antrum must be preserved. Truncal vagotomy, which is combined with a drainage procedure, should, therefore, be avoided. Immediately after vagotomy co-ordination and propagation of the gastric electrical control activity is disrupted and antral peristalsis impaired (Wilbur and Kelly, 1973). Antrectomy would also increase the rate of emptying of solids. It would appear, therefore, from the point of view of motility, that proximal gastric vagotomy causes minimum disruption of the antral duodenal relationship and of the contractional activity of the antrum. It should be considered at present as the most physiological operation for surgical management of peptic ulcer disease.

SUMMARY AND CONCLUSION

The present investigation was the first attempt to study the effects of pylorectomy on gastric emptying, antral motility and myoelectrical activity and to measure transit and motility

simultaneously. The findings and conclusions are:

1) That the rate of gastric emptying is primarily related to antral motility. Duodenal motility does not appear to play a major role.

2) In the intact animal there is no co-ordination between myogenic electrical activity in the antrum and duodenum during fasting periods, but the electrical activity becomes co-ordinated after meals. The post-prandial co-ordination is abolished after removal of the pylorus. From this study it could not be ascertained whether this loss of co-ordination was due to disruption of myogenic or neural pathways.

3) Duodenal motility is inhibited during feeding periods. This absence of electrical response activity and contractions also occurs during feeding periods after pylorectomy. Although it is tentatively proposed that this inhibition involves extrinsic neural pathways, this remains unproven.

4) Although it was expected that removal of the pylorus would lead to a decrease in transit time from stomach to duodenum, it was found that the transit of solids or of liquids was not significantly affected by pylorectomy.

5) Interdigestive migrating myoelectric complexes were recorded from the duodenum before and after pylorectomy, but were recorded from the antrum only prior to removal of the pylorus.

6) That the pylorus is not a tonically contracted sphincter, opening occasionally, but that it behaves as the distal end of the thickened muscle mass surrounding the antrum and is part of that single muscle unit.

CHAPTER V

TACHYGASTRIA

Tachygastria, as described by Code and Marlett (1974), is characterized by a sequence of electrical control activity at abnormally rapid frequencies. In their two dogs these rapid frequencies persisted for a minute or more and in one instance, lasted as long as 32 minutes. Orad propagation of the abnormal electrical control activity was observed at times.

The dog (G 293) in our series was eliminated from the original experiment and studied separately because of persistent tachygastria. This is the first case of persistent canine tachygastria ever to be described or indeed to have been studied for any length of time.

TYPES OF ARRYTHMIAS

Two abnormalities in rhythm were identified in this dog. One was classified as Burst Activity and the other as Tachygastria.

Burst Activity. This consisted of bursts of activity first detected by the strain gauge on the antrum and then recorded almost simultaneously by both antral electrodes and duodenal strain gauges and electrodes (Figure XXVIII). These bursts occurred every 7 - 8 minutes while fasting, during feeding, and post-prandially. They were present irrespective of the time of day in which recordings were taken, and

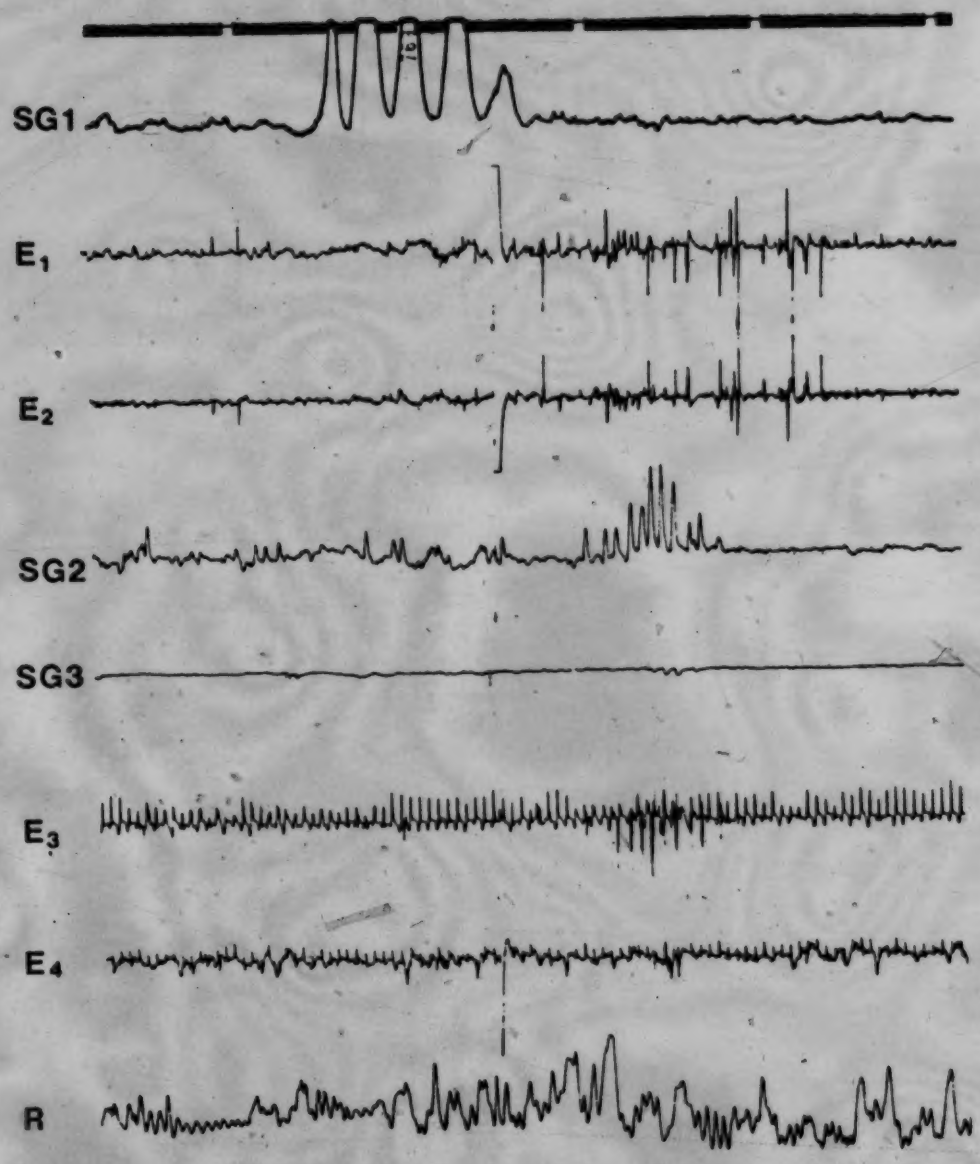

FIG. XXVIII. BURST ACTIVITY RECORDED FIRST BY ANTRAL STRAIN GAUGE AND THEN BY ANTRAL AND DUODENAL ELECTRODES AND DUODENAL STRAIN GAUGE. S.G.1 - ANTRAL STRAIN GAUGE; E_1 AND E_2 - ANTRAL ELECTRODES; S.G.2 AND S.G.3 - DUODENAL STRAIN GAUGE; E_3 AND E_4 - DUODENAL ELECTRODES. R - RESPIRATION. TIME MARKER INDICATES SECONDS AND MINUTES.

were also present following pylorectomy.

Tachygastria. This was characterized by abnormally fast antral electrical control activity which was omnipresent prior to pylorectomy (Figure XXIX). The frequency of the antral electrical control activity ranged from 18 to 20 cycles/minute. When compared to the frequency and waveform of the duodenal electrical control activity during anaesthesia in normal dogs a very similar pattern was seen (Figure XXX).

Direction of Propagation. The direction of propagation of the antral electrical control activity in this dog, during tachygastria, was in the orad direction.

RESULTS

Gastric Emptying. I was fortunate to have studied gastric emptying in this dog. Before removal of the pylorus gastric emptying of both liquids and solids was abnormally slow, when compared to normal dogs. In the tachygastric dog, < 20% of fed PEG was emptied in 90 minutes, compared to 65% in control dogs. A similar finding was present for ^{99m}Tc; < 20% of total ingested radiolabelled solids were emptied in 90 minutes compared to 60% in control animals.

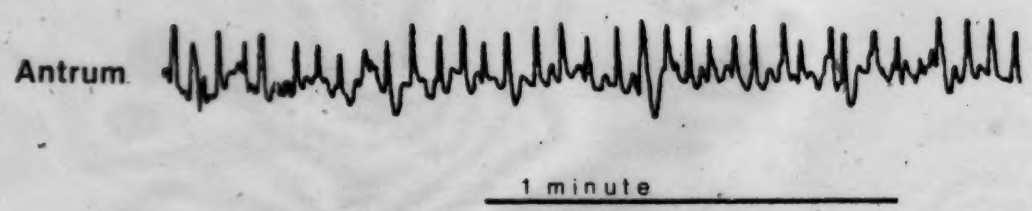

FIG. XXIX. ANTRAL TACHYGASTRIA SHOWING ANTRAL ELECTRICAL CONTROL ACTIVITY 18 - 20 CYCLES/MIN.

FIG. XXX. ANTRAL TACHYGASTRIA AND DUODENAL ELECTRICAL CONTROL ACTIVITY RECORDED DURING ANAESTHESIA.

Effects of Pylorectomy. There was an apparent increase in emptying rate following pylorectomy (Figure XXXI and XXXII). The emptying rate in 90 minutes for PEG was now 87% and for ^{99m}Tc was 70%. Prior to pylorectomy this animal was listless, vomited occasionally, and was an extremely poor feeder. In the immediate four weeks following operation, however, there was a remarkable increase in appetite and general condition combined with an increase in weight from 18.3 Kg. to 26.3 Kg., a total of 8 Kg.

Pylorectomy and Antral Electrical Activity. Following pylorectomy, the pattern of the antral electrical activity resumed a more normal waveform and returned to a frequency of 4 to 5 cycles/minute (Figure XXXIII). The propagation of the antral electrical control activity also returned to an aborad direction.

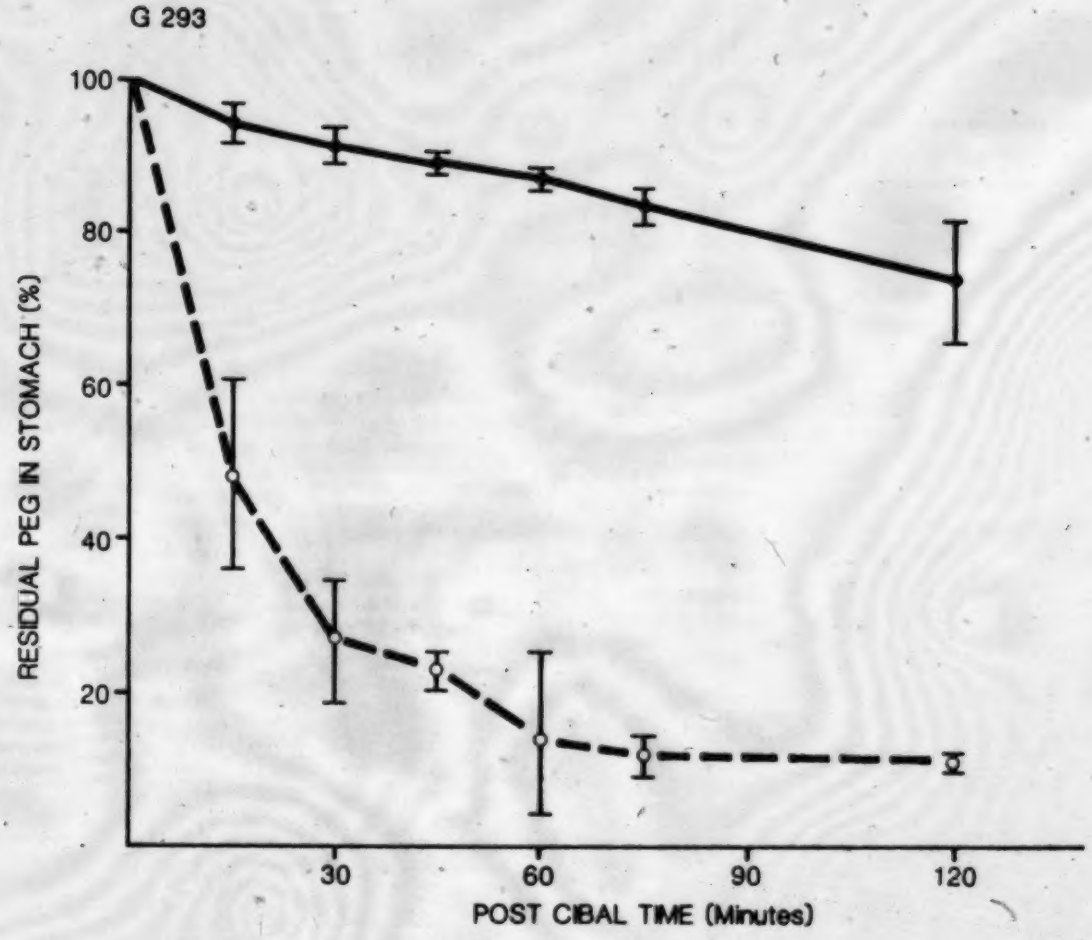

FIG. XXXI. EMPTYING OF PEG IN TACHYGASTRIC DOG.
●————● BEFORE PYLORECTOMY;
o----------o AFTER PYLORECTOMY.
EACH POINT REPRESENTS THE MEAN OF 4 OBSERVATIONS.

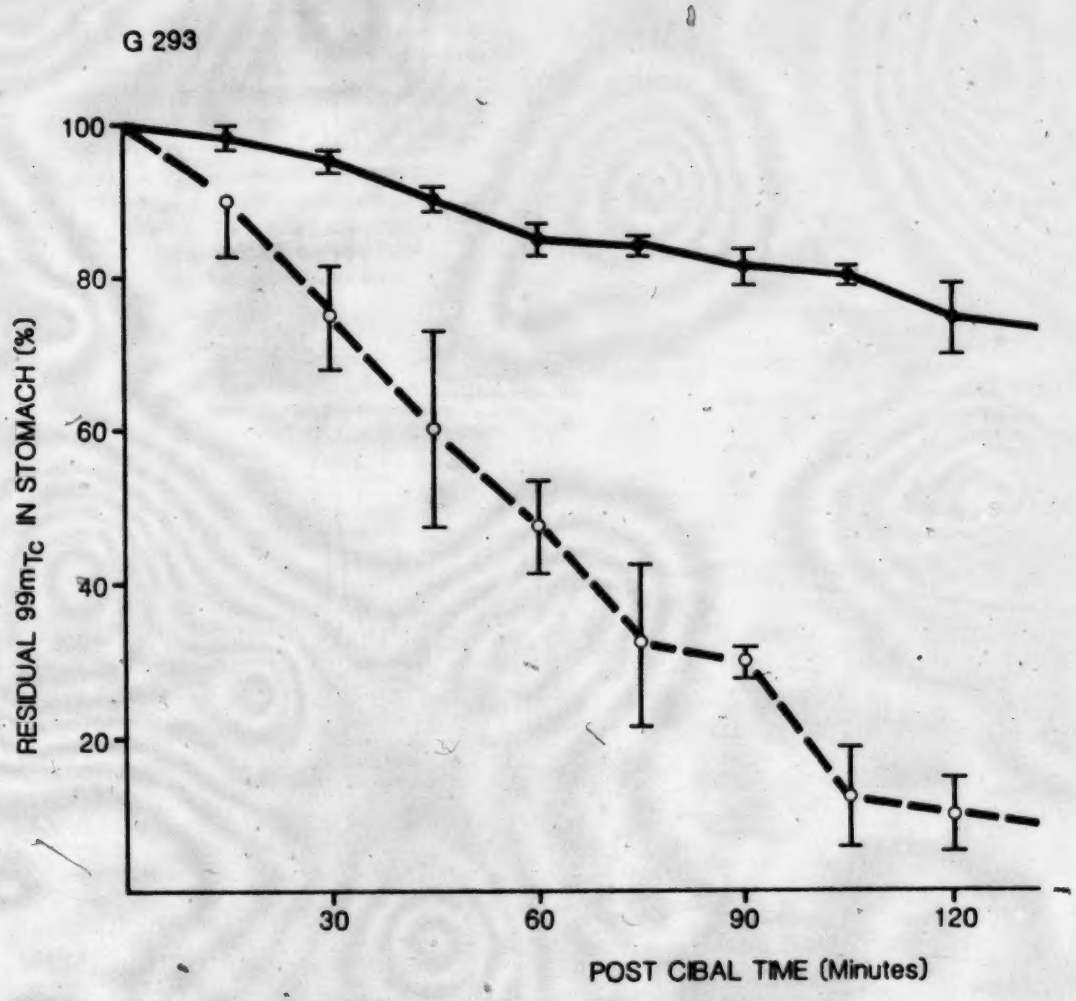

FIG. XXXII. EMPTYING OF ^{99m}Tc IN TACHYGASTRIC DOG.
●————● BEFORE PYLORECTOMY;
o----------o AFTER PYLORECTOMY.
EACH POINT REPRESENTS THE MEAN OF
4 OBSERVATIONS.

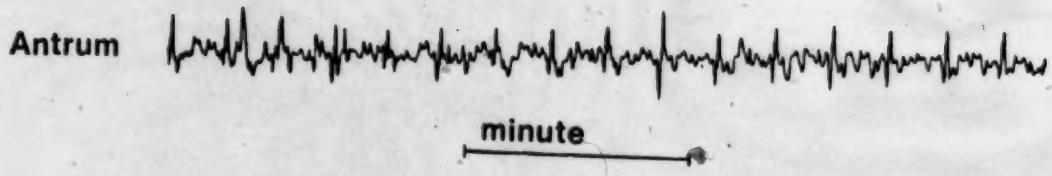

FIG. XXXIII. ANTRAL ELECTRICAL CONTROL ACTIVITY IN TACHYGASTRIC DOG FOLLOWING PYLORECTOMY. RATE 4-5 CYCLES/MIN.

DISCUSSION

The gastric electrical control activity originates in a saddle-shaped area, the pacemaker, which sits astride the greater curvature at the junction of its orad and middle thirds. From here the electrical control activity sweeps distally through the longitudinal muscle fibres to the pylorus where it ends (Kelly and Code, 1971). Its frequency in dogs is 4 - 6 cycles/minute, in humans 3 cycles/minute. In its spread over the stomach the gastric electrical control activity, like the cardiac, prescribes the direction and rate of propagation.

The frequency of the abnormal antral pacesetter potential in this dog was 18 - 20 cycles/minute. It is thought that the abnormal drive might have originated from the pacemaker of the duodenum and that the duodenal electrical control activity was being conducted orad, across the pylorus, into the antrum. This would also account for a return to a more normal pattern in the antrum following excision of the pylorus. However, the antral tachygastria was never in phase with the duodenal pacemaker; indeed, the tachygastria never was of the exact same frequency. The tachygastria, therefore, must be due to the presence in the antrum of an abnormal pacemaker. Its frequency in this dog was almost four times faster than that of normal gastric electrical control activity. The abnormal pacemaker thus, as a result of its higher frequency, over-rides the normal physiological pacemaker. This

also accounted for the orad propagation which occurred.

Code and Marlett (1974), have described disappearance or dissolution of antral arrythmia and tachygastria as soon as electrical response activity occurs. There is no indication that normal gastric contractions involve arrythmia or tachygastria. If this did occur gastric emptying would be altered. This is precisely what occurred in this dog. The tachygastria persisted even in the presence of electrical response activity and this accounted for the very slow gastric emptying rate.

Whether the antral tachygastria extended to the corpus in this animal is not known, since recording electrodes were not present. The rate of propagation of the normal gastric electrical control activity is more rapid in the antrum than in the corpus, and the antrum can sustain faster electrical control activity than can the rest of the stomach (Kelly et al., 1969; Carlson et al., 1966). While the normal cells in the corpus could not follow the abnormally fast antral electrical control activity, it must be presumed that some influence associated with tachygastria did reach these more orad cells.

On excision of the pylorus in this dog, the emptying rate returned to an apparently more normal pattern. The conclusion must be drawn that the ectopic pacemaker was located in the muscle which was removed during operation. Could this condition in man account for the non-functional gastric syndromes described?

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